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JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 5 1951

THE PHYSIOLOGY OF NEUROMUSCULAR TRANSMISSION AND NEUROMUSCULAR BLOCK*

BY

W. FELDBERG, M.D., F.R.S.

(From the National Institute for Medical Research, Mill Hill, London, N.W.7)

When we talk to-day about neuromuscular transmission we have an advantage over anyone who spoke about this subject ten or even five years ago. Even five years ago we should have had to spend a substantial part on the question, Is acetylcholine the chemical transmitter from motor-nerve endings to skeletal muscle ? We could, and certainly would, have made out an extremely strong case for acetylcholine, but the difference between then and now is not how strong the case has become in the meantime, but that the case, as a matter of dispute, is settled and no longer exists. I think it is no exaggeration to say that to-day the acetylcholine theory of neuromuscular transmission has been universally adopted.

What, however, about the other two transmission processes that have so often been grouped together with neuromuscular transmission—the transmission in a sympathetic ganglion and across the central synapse? For the sympathetic ganglion the position can be stated as follows. No one denies that here, too, a strong case can be made out for acetylcholine ; but some ask, Is acetylcholine the whole story, or may the electrical variation of the nerve impulse be involved in the transmission process as well ? This is what Bronk (1939) has called the pluralistic view. Recently Lorente de Nó and Laporte (1950) have published a monograph of nearly 200 pages on synaptic transmission in a sympathetic ganglion. They report mainly on their own experiments, but in fifteen lines they deal with the nature of the synaptic transmitter, or rather with the controversy on the nature of the transmitter. In their view the chemical theory in its present form cannot account for all their electrophysiological findings in the ganglion, and they therefore ask: Must we discard the chemical theory or can it be elaborated so as to explain the new findings ? They conclude, " It is undoubtedly best to be thoughtful." So, whatever my personal views on this matter, for some at least the case is still pending.

When we come to the central nervous system the opposition against the acetylcholine theory is even stronger. About two years ago I spoke about this problem.† The conclusion was reached that the evidence so far available did not allow us to assume that acetylcholine was the universal central synaptic transmitter, but that it suggested that acetylcholine exerted such a function at numerous central synapses. What I actually did was to put before you all the evidence I could find in favour of acetylcholine as a transmitter in the central nervous system. In other words, I stated the case for the defence of acetylcholine.

I think the general acceptance of the acetylcholine theory in neuromuscular transmission is based not only on the overwhelmingly positive evidence, such as, for instance, that acetylcholine is released on motor-nerve stimulation, that injections of acetylcholine can imitate all details of motor-nerve stimulation, and that there is at the neuromuscular junction a concentration of the enzymes which synthesize and destroy acetylcholine ; but also on what I may call the negative evidence—that is, whenever the possibility existed to try out whether the nerve impulse could cause contraction without acetylcholine the answer was no, the nerve impulse was unable to do so.

1. Evidence that the Nerve Impulse without Acetylcholine is Apparently Unable to Cause Contraction

What is so interesting is the fact that what I termed " the negative evidence " had actually been provided long before the acetylcholine theory had been suggested. In 1904 Langley and Anderson united different kinds of nerves and studied the results of nerve regeneration. They connected, for instance, to the distal stump of the sciatic the central end of the cut sensory saphenous nerve, which, as we now know, is a non-cholinergic nerve. Thirteen months later they stimulated electrically the distal end of the sciatic stump and observed a reflex response in the animal but no contractions of the muscles supplied by the sciatic. The reflex response proves that the sensory-nerve fibres must have grown into the sciatic, but the absence of contractions shows that they had been unable to form functional connexions with the muscle. At that time the various results obtained by Langley and Anderson must have been rather bewildering. For instance, why, if a sensory fibre on regeneration into a motor stump was unable to achieve functional innervation with a muscle, could a preganglionic sympathetic fibre do so ; and why, on the other hand, could this same fibre not make functional connexion with the post-ganglionic sympathetic fibre ?

*Lecture given on October 16, 1950, at the Neurological Institute, National Hospital, Queen Square, London, and on November 22, 1950, in the Department of Pharmacology, Oxford University.

†The contents of the lecture have been published elsewhere (Feldberg, 1950).

It was left to Dale (1935) to show what these results meant. Langley and Anderson had found that nerve fibres grow into any nerve stump, but can make functional connexions only if they are of the same nature—that is, only cholinergic fibres can make functional connexion with cholinergic fibres, sensory only with sensory, adrenergic only with adrenergic, not sensory with cholinergic, nor cholinergic with adrenergic, and so on.

It may be asked how we know that in Langley and Anderson's experiments the sensory fibres had actually reached the muscle fibres, so that we are justified in concluding that the nerve impulse had got to the muscle fibre but could not make it contract. Such histological evidence was given by Weiss (1935) and by Weiss and Edds (1945).

Weiss, working with toads, implanted the cut ends of sensory roots direct into denervated muscles. Histological examination showed that the sensory fibres had spread throughout the muscle fibres. Nevertheless, in most of their experiments electrical stimulation of the sensory nerve did not cause contraction of the muscle. When it did, the intrusion into the wound of stray motor fibres of uncontrollable origin could be made responsible for it. This complication was later avoided in the experiment of Weiss and Edds. They worked with rats and used a special method of uniting sensory and motor nerves. Union was effected without suture by inserting the opposing nerve ends into fitting sleeves made from an artery of another, freshly killed, young rat. They established, without doubt, that sensory–motor union does not enable the sensory regenerating nerve fibres to make the muscle contract, although histological examination proves that they have grown in normal fashion through the motor stump and have pervaded the muscle with extensive arborizations which would provide ample opportunity for the establishment of myoneural junction if, as we may say, these fibres would only liberate acetylcholine.

I am aware that one can argue against this conclusion, and that it can be said that the cause for the failure of transmission is not lack of acetylcholine but an inadequacy of structural connexions between the sensory endings and muscle. I wonder, however, if this objection has any real meaning. The sensory fibres have reached the muscle and we must realize that there is no difference in electrical excitability between different parts of a muscle fibre, not even between motor end-plate and muscle fibre, as was shown by Kuffler (1945). If lack of acetylcholine is the determining factor, any structural connexion without acetylcholine can be called inadequate.

Another instance which illustrates that a nerve impulse may reach a muscle without exciting it is found in crustacea. In these animals some limb muscles have a double innervation, motor and inhibitor; both nerves run closely together, and their common course can be followed down to fine intramuscular branches. The motor response is abolished or prevented by stimulation of the inhibitory axon. We do not know what the transmitter of even the motor axon is. In fact, the evidence so far available speaks against acetylcholine (see Katz and Kuffler, 1946; Welsh and Schallek, 1946; Bacq, 1947; Katz, 1936, 1949; Hunt and Kuffler, 1950b). The fact of interest for our argument is that when the inhibitory axon is stimulated to a resting muscle no muscular contraction occurs. The only visible response is a small intramuscular nerve spike, looking exactly like a motor-nerve spike, but this intramuscular nerve spike does not excite the muscle, or, expressed in more electrophysiological terms, the current spread of the nerve impulse is ineffective on the muscle (Katz and Kuffler, 1946).

One more example, to show that current spread from the nerve endings is apparently unable to produce the change at the motor end-plate which leads to excitation of the muscle fibres. This change is a depolarization. There is a definite but extremely small time-lag between the arrival of the nerve impulse and the depolarization of the end-plate—the so-called neuromuscular or end-plate delay. In the past this delay played a prominent part as an argument against the acetylcholine theory, the argument being that this time was far too short to account for the release of acetylcholine and its subsequent action on the end-plate. But now the opposite view is taken. Kuffler (1948) measured this delay in frog muscle. He stimulated, not the nerve trunk at some distance from the muscle, but the terminal nerve region only about 0.5 mm. away from the end-plate. If spread of current were the transmitter of the nerve impulse, depolarization of the end-plate should have been effected within a fifth of a millisecond. But it took about the whole of a millisecond. Four-fifths of a millisecond remained unaccounted for, and these four-fifths of a millisecond are now presented as evidence against the electric current from the nerve terminals being the transmitter agent.

I shall once more return briefly to this problem, and give another instance of indirect evidence that a brief electrical shock is apparently an ineffective mechanism for depolarization of the end-plate.

2. Action of Acetylcholine at the Motor End-plate

As acetylcholine is the transmitter of motor-nerve impulses, any condition which affects neuromuscular transmission must be interpretable in terms of acetylcholine. Obviously, a clear understanding of its action is necessary.

Acetylcholine has three actions on skeletal muscle. First, it may cause contraction; secondly, it may produce depression—that is, neuromuscular block; and, thirdly, it may cause a contracture. And all three actions are apparently the result of one effect of acetylcholine—that of depolarizing the motor end-plate. Acetylcholine has no action on the muscle fibre itself, or, I should be more cautious and say, no action which concerns neuromuscular transmission, because effects of acetylcholine on muscle metabolism have been observed (Gollwitzer-Meyer, 1950).

The Acetylcholine Contraction

For describing the action of acetylcholine on the motor end-plate a simple diagram like that shown in Fig. 1 is helpful. The acetylcholine released from the nerve endings depolarizes the membrane of the motor end-plate as indicated in the diagram. This depolariza-

FIG. 1.—Diagram of muscle fibre with end-plate. Nerve fibre ends on end-plate, which becomes depolarized (indicated by dots) by the released acetylcholine.

tion is the appropriate stimulus to excite the muscle fibre, so that an excitation wave travels along the fibre and elicits the contraction. The acetylcholine is quickly hydrolysed, and therefore the motor end-plate is no longer depolarized when the excited muscle fibre has come out of its refractory state, so a single nerve impulse elicits no second wave of excitation. That, however, occurs after eserine, or with an injection of a small dose of acetylcholine into the muscle artery. In other words, the response of the eserinized muscle to a single nerve impulse is no longer a twitch, but a summated contraction, a short tetanus; and the contraction due to an arterial injection of acetylcholine is also a short tetanus, but this time an asynchronous one. The tetanus in both cases results from persistence of acetylcholine at the one

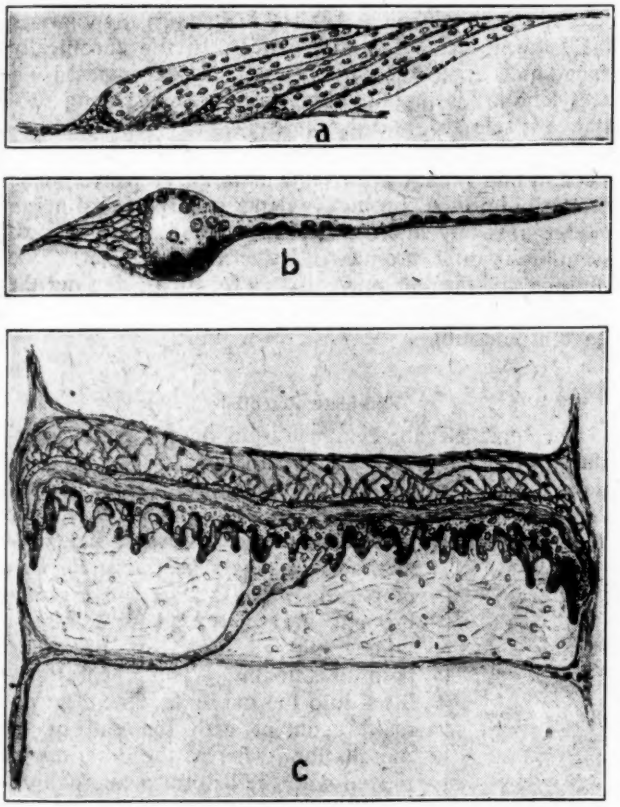

FIG. 2.—Different stages in the development of the plates of an electric organ. (*a*) The early stage: muscle fibres with faint cross-striation are still predominant. Five muscle fibres with end-plate regions on the upper end of the four fibres. (*b*) Later stage: a single fibre. End-plate region has increased in size. (*c*) Fully developed single plate. Rudiment of muscle fibre still discernible: in many fully developed plates it is completely absent. From the arrangement of the muscle fibres and plates at (*a*) the final arrangement of the plates in columns built up of superimposed plates becomes evident. (After Ewart.)

end-plate region long enough to keep it depolarized for re-excitation of the muscle fibre after it has come out of its refractory state.

The depolarization of the end-plate is not a theory, but it can be demonstrated; it is termed the motor end-plate potential. End-plate potentials can be recorded from the end-plate region of a muscle, or we may use a preparation which consists of end-plates only. Such a preparation is the electric organ of the torpedo fish.

The Depolarizing Action of Acetylcholine on the Electric Organ of the Torpedo

The organ is an accumulation of modified hypertrophied end-plates derived from skeletal muscle but

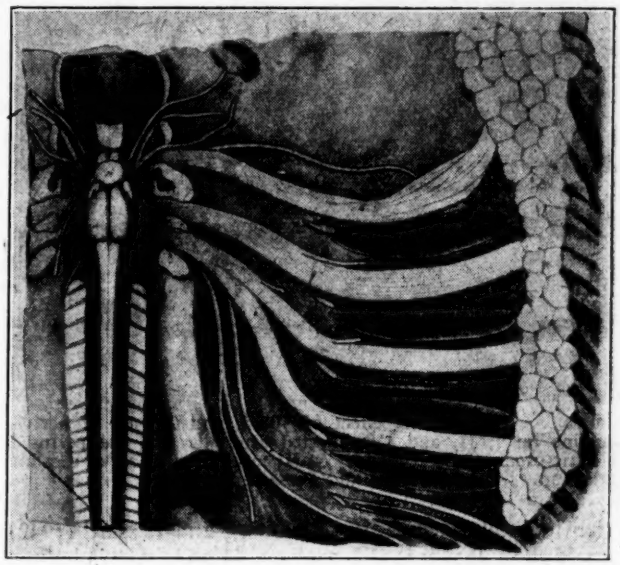

FIG. 3.—Diagram of an electric organ in the torpedo with its large extrinsic nerves.

lacking the contractile element. Before the organ is fully developed it consists of striated muscle fibres which have their end-plate not in the middle of the fibre, as usual, but at one end. This end grows until a fully developed plate is obtained, whereas the small muscle fibre remains either unchanged, diminishes, or disappears. In Fig. 2 are shown the different stages in the development of a plate, whereas Fig. 3 gives a schematic illustration of the arrangement of the whole electric organ. It is formed by a great number of columns arranged side by side, each column being built up of several hundred superimposed plates. Large efferent nerves enter the plates from the ventral sides, covering them with a terminal nerve net. Impulses are sent down from the central nervous system along the nerves, causing a brief discharge of the organ. A photograph of a torpedo fish on which an experiment was done is given in Fig. 4; the left organ has been removed and is shown at *b* with its large nerves. The blood vessels run with the nerves and the organ can be perfused from its cannulated artery.

Marnay (1937) and later Nachmansohn and Lederer (1939) had found that the electric organ is extremely

FIG. 4.—(*a*) Torpedo fish with left electric organ removed. (*b*) Removed electric organ with large extrinsic nerves.

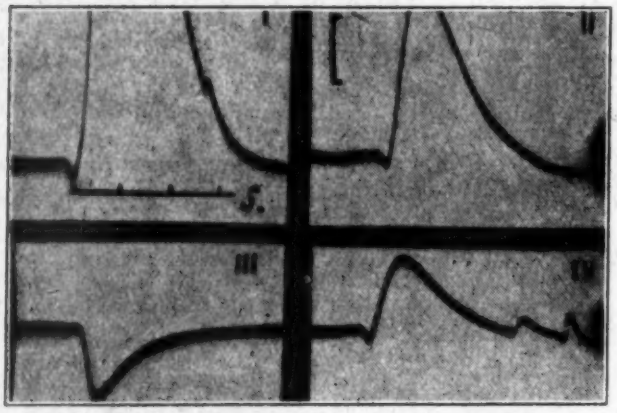

FIG. 5.—Depolarizing effect of 10, 5, and 2.5 μg. of acetylcholine (at I, II, and IV) injected arterially into the perfused electric organ of the torpedo. At III mechanical effect of a saline injection. (After Feldberg and Fessard, 1942.)

rich in cholinesterase, and Feldberg and Fessard (1942) could show that it is also extremely rich in acetylcholine, and that acetylcholine is released by stimulating the nerve to the perfused organ. Fessard and I then proceeded to find out if acetylcholine has an electrogenic effect, and for that purpose we injected acetylcholine arterially into the perfused organ. The result is seen in Fig. 5, which shows the strong depolarizing or electrogenic effect of small doses of acetylcholine. The small deviation downwards, when saline alone is injected (at III), is due to the mechanical disturbance of the injection. The potentials due to the depolarizing action of the acetylcholine occur after a short latency.

I can now give the additional evidence I mentioned before—why, in my opinion, a short electrical shock is an ineffective stimulus for depolarization of the end-plates.

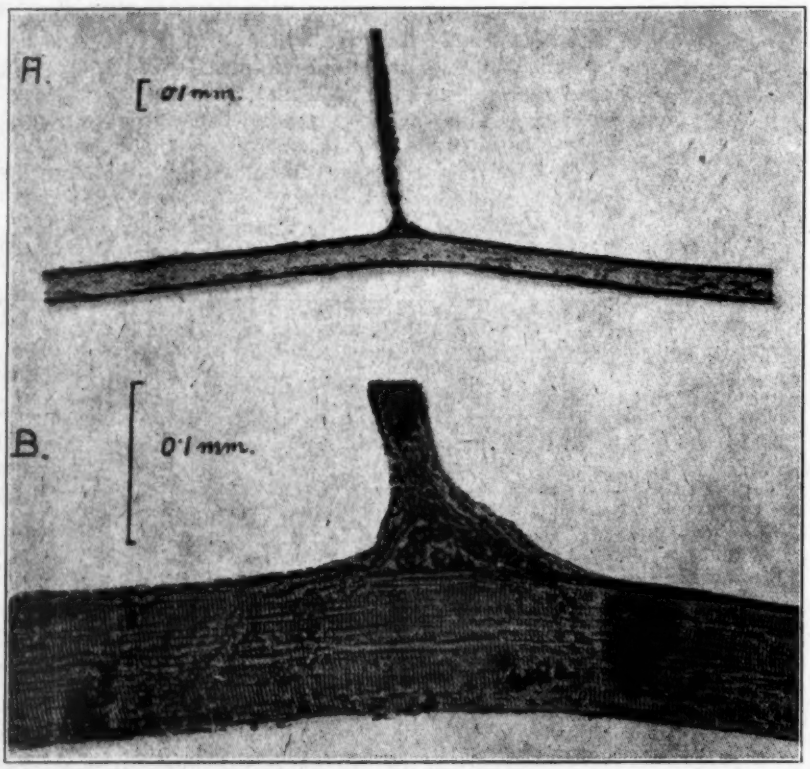

FIG. 6.—Photomicrograph of a living single muscle fibre with its nerve supply. A, Low magnification. B, Higher magnification. Dark area to the right of the nerve-entry is a small air bubble. (After Kuffler, 1942.)

The isolated electric organ of the torpedo can be stimulated artificially, for instance, by pressing on it with an ivory rod, or by an electric current. The response is a discharge which, on electrical stimulation, is clearly distinguishable by a short latency from the artifact of stimulation. But the position is different when the nerves to the organ have been severed and have degenerated. Then a discharge is no longer obtainable whatever stimulus we apply. Even an electric shock gives only the artifact of the stimulus without subsequent discharge. This was known to Garten (1910), and has been confirmed more recently by Auger and Fessard (1938).

The following explanation is suggested. In normally innervated organs any stimulus, mechanical or electrical, will excite the intraplatal nerve fibres; this leads to release of acetylcholine, which, in its turn, depolarizes the ventral surfaces of the plates. In the chronically denervated organ the nerve fibres have degenerated, no acetylcholine is present, therefore no depolarizing substance is released, and the electric shock itself is ineffective in depolarizing the plates. To prove this theory Fessard and I made arrangements to inject acetylcholine arterially into the chronically denervated perfused organ to see if acetylcholine, the appropriate physiological stimulus, would produce its electrogenic effect. The outbreak of the war prevented us from carrying out the experiment, about the outcome of which, however, I have little doubt.

End-plate Potentials

The most elegant demonstration of end-plate potentials in muscle, which are essentially the same potentials as those in the electric organ, is that of Kuffler (1942, 1943). He worked on isolated nerve muscle fibres of the frog, and used the following ingenious method. A single nerve-muscle fibre preparation, like that seen in Fig. 6, is brought into a trough containing a saline solution, on top of which paraffin is floating. The preparation is lifted into the paraffin. One electrode makes contact with the end of the muscle fibre, whereas the other can be moved with the help of a microadjustment to different positions along the fibre. Kuffler used a little glass rod terminating in a hook, in the loop of which this second electrode is fixed. The loop also holds a fine droplet of diluted solution of acetylcholine (Fig. 7.) Under direct microscopical observation, the hook is lowered to the end-plate region. The result is a local depolarization of this region which, if strong enough, leads to propagated

FIG. 7.—Diagram illustrating local application of acetylcholine to an isolated muscle fibre, M (transverse section). G, Glass rod terminating in a fine hook. Shaded area shows droplet of acetylcholine which is brought into contact with the muscle fibre by lowering the glass rod (arrow). (After Kuffler, 1942.)

impulses along the muscle fibre. Fig. 8 is taken from the paper by Kuffler and shows the effects of acetylcholine applied in this way to the end-plate region. At *a* the depolarization by acetylcholine sets up four propagated impulses, but at *b* depolarization is too weak to excite the fibre; only the slow motor end-plate potential

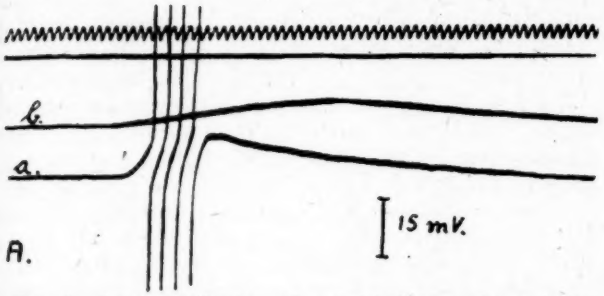

FIG. 8.—Local application of acetylcholine to the end-plate region of a single nerve-muscle fibre preparation. Recording is done from the point of application. *a*, 10^{-6} Acetylcholine sets up four propagating muscle impulses. *b*, A weaker concentration of acetylcholine produces a local negative potential only. Time scale: 1 div. = 10 msec. (After Kuffler, 1942.)

is recorded. Such a potential can be obtained only when led off directly from the end-plate region; when the leading-off is a few millimetres away we get only propagated impulses as illustrated in Fig. 9. Further, acetylcholine produces no effect when applied to the muscle fibre away from the end-plate region.

To record end-plate potentials in mammalian muscle either by acetylcholine given artificially or by the nerve

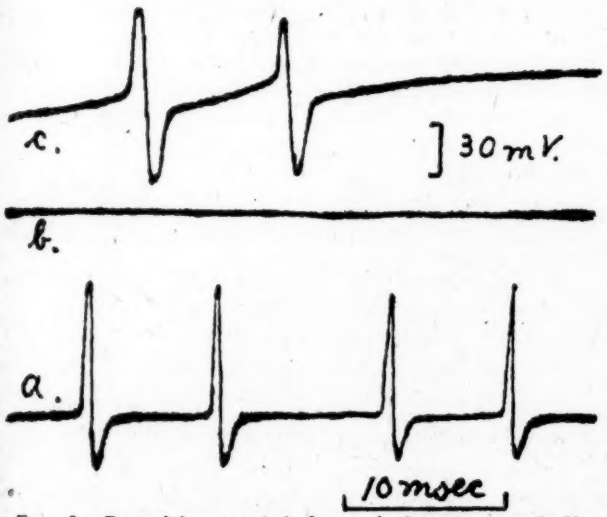

FIG. 9.—Potentials recorded from single nerve-muscle-fibre preparation. *c*, Acetylcholine applied to end-plate, while the recording is done from point of application (as Fig. 8, but faster sweep). *a*, Impulses initiated at end-plate are recorded 5–6 mm. away from it. Note the absence of a negative potential preceding or following the spikes. *b*, Base line. (Redrawn from Kuffler, 1942.)

impulse has become simple by the use of curare preparations for this purpose, introduced by Eccles and his co-workers (Eccles and O'Connor, 1938, 1939; Eccles, Katz, and Kuffler, 1941). D-Tubocurarine reduces the acetylcholine effects on the end-plates so that depolarization is insufficient to excite the fibres but still sufficient to be recorded. Fig. 10 illustrates end-plate potentials produced by a single nerve volley in curarized cat's muscle. Again, in order to obtain the potentials it is necessary to lead off directly from the end-plate region, because this depolarization is not propagated, or, as it is termed, it spreads decrementally for a few millimetres only on either side of the end-plate.

The events which occur on the arrival of the motor-nerve impulse at its terminals thus are: nerve impulse—release of acetylcholine—depolarization of the end-plate—excitation of the muscle fibre. The excitation is

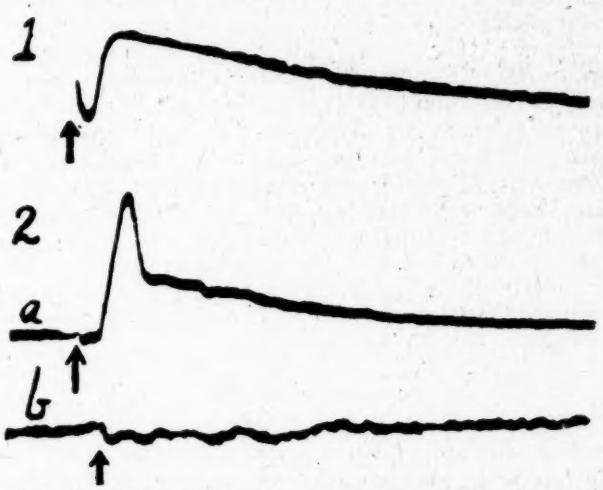

FIG. 10.—Action potentials to a single nerve impulse from end-plate region of cat's soleus muscle. (1) Full curarization: shows the slow end-plate potential alone. (2) Less curarization: at *a* the spike response at the end-plates; at *b* no potential when led off 2 cm. away from the end-plates. No contraction. (After Eccles and O'Connor, 1938.)

propagated and leads to contraction of the contractile elements. When we discuss contraction of muscle fibres we have to distinguish, as emphasized by Katz and Kuffler, between the two processes—excitation of the muscle membrane, the action potential, and activation by it of the contractile substance, the contraction.

Release of Acetylcholine from the Resting Nerve

There is this problem: is acetylcholine released only by the arrival of the nerve impulse, and is there a completely resting condition between nerve impulses? I do not think so.

We may compare the release of acetylcholine with what happens at a sluice or lock, where there is always some leakage even when the lock is closed. The amounts of acetylcholine released at rest, however, are far too small to produce effective transmission so long as the mechanism for the destruction of acetylcholine is intact. This idea is based on the effect of eserine, which causes fascicular twitching and fibrillation even after cutting the nerve. The fascicular twitchings may be accounted for by the release of acetylcholine by random impulses passing down the cut nerve. The fibrillations cannot be explained in this way. They might be due to continuous release and resynthesis of minute amounts of acetylcholine from the endings of the resting nerve, so slight as to have no effect in the absence of eserine (Feldberg, 1945). There is a fact which could be strikingly explained on this assumption: eserine loses its ability to produce these motor effects one to two days after cutting the nerve, although the motor end-plate remains sensitive to acetylcholine and the nerve still conducts. The only change which has occurred at this time is an impairment of the nerve fibre to synthesize acetylcholine. The acetylcholine content of the nerve has dropped and the tissue synthesizes acetylcholine in small amounts only. Therefore even after eserine no effect is to be expected.

The analogy of the sluice has recently found a more scientific and exact explanation. Fatt and Katz (1950) inserted a micro-electrode immediately under the motor-nerve ending of a frog muscle fibre and observed, without stimulating the nerve, small action potentials which followed one another at random intervals and were of the size of 1% of the normal end-plate potential. These were increased by neostigmine and abolished by D-tubocurarine; they were termed "miniature end-plate potentials." Fatt and Katz gave the following explanation of their origin. The fine nerve terminals are excited by spontaneous fluctuations of their membrane potential; the nerve terminals are so thin that this local excitation will not lead to a propagated impulse along the whole nerve, the area affected being too small; but it will lead to the release of a minute amount of acetylcholine, which then produces the miniature end-plate potential which, again, is subthreshold to excite the muscle fibre. So the idea of a resting state at the nerve endings has to be relinquished.

Depression by Acetylcholine

The depression obtained with acetylcholine occurs either when large doses of acetylcholine are injected into a muscle or when the nerve to an eserinized muscle is frequently stimulated. Fig. 11 illustrates a tension

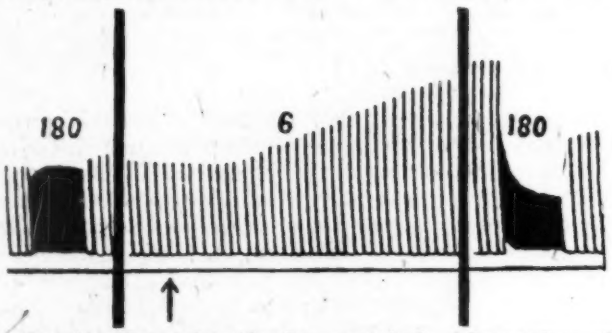

FIG. 11.—Cat under chloralose anaesthesia. Contractions of tibialis anterior in response to maximal shocks to nerve at frequency of either 6 or 180 a minute. At arrow, intravenous eserine 0.5 mg. per kg. body weight. The dark patches are caused by overlapping of the individual contractions during high-frequency stimulation. (After Bacq and Brown, 1937.)

record of a cat's muscle stimulated from its motor nerve either with single impulses placed at 10-second intervals or with frequent stimulation. At the arrow, eserine is given. The response to the single impulses is augmented and converted into a short tetanus, as mentioned before, but tetanic stimulation is reduced. Fig. 12 illustrates the reduction in the response of single nerve impulses when an arterial injection of acetylcholine or a short tetanus is interpolated. The depression in both experiments is the result of too much acetylcholine, and has in the past often been called the "curare-like action of acetylcholine"—a classification which, as we shall see, is misleading.

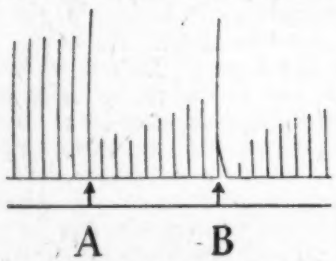

FIG. 12.—Spinal cat. Contractions of gastrocnemius muscle in response to single maximal shocks to nerve at 10-second intervals, after arterial injection of 0.1 mg. of the anticholinesterase miotine. A, Arterial injection of 10 μg. of acetylcholine. B, Short tetanic stimulation of nerve. (After Bacq and Brown, 1937.)

Originally, I had the idea that this effect, which occurs when the muscle is, so to speak, flooded with acetylcholine, was an action of acetylcholine on the muscle fibre (Feldberg, 1950). This idea may be wrong. Acetylcholine apparently acts only on the end-plate, as recently shown by Burns and Paton (1950). But when the acetylcholine persists here long enough, then not the acetylcholine but the depolarization current spreads to the adjacent parts of the muscle fibre, which also become depolarized, and when part of a muscle fibre becomes depolarized, not for a brief moment but for some time, this part becomes electrically inexcitable—that is, an excitation wave cannot pass this region, therefore a nerve can no longer excite the muscle fibre—neuromuscular block has been established.

Burns and Paton have measured the depolarization by acetylcholine in the cat's gracilis muscle, which is a simple muscle with localized end-plate regions and nerve-free distal parts. They used the following technique. The electrode sweeps to and fro over the muscle. Normally there is no change in the state of depolarization during such a sweep, but when acetylcholine has previously been injected into the muscle artery—or, better, another substance of which we shall speak more later on, decamethonium—then each time the electrode approaches an end-plate region a depolarization current is recorded. When the sweep is repeated a few minutes later it is found that the depolarized region has become larger: the depolarization apparently has spread along the muscle fibre on either side of the end-plate; thus the region depolarized is no longer confined to the end-plate. This is the most likely explanation of the depressant action of acetylcholine. But we cannot exclude the possibility that persistent depolarization of the end-plate region itself produces a condition of depression which, for instance, occurs even in the electric organ of the torpedo after eserine, although this organ lacks the muscle fibres.

The Acetylcholine Contracture

In mammalian muscle, depolarization of the muscle fibre on either side of the end-plate leads only to depression. In the frog such depolarization is associated with another phenomenon—contracture. From the point of excitation, contractures—that is, non-propagated contractions—and depression are the same. In both conditions the muscle is electrically inexcitable at the depolarized region. This, in mammalian muscle, is the sole effect, and the cause of neuromuscular block. In frog muscle it produces a slow shortening of the muscle, the contracture. But essentially there is no difference between the normal mammalian muscle and the frog muscle. After motor denervation of a mammalian muscle, depolarization of the muscle membrane by acetylcholine produces strong contractures in this muscle also. It is possible that even in the normal muscle persistence of acetylcholine produces a very slight local contracture of the muscle fibre directly near the motor end-plate region, but too small to be recorded with our normal tension records; it will, however, naturally produce block. In fact Brown, Burns, and myself (1948) observed that an arterial injection of acetylcholine after di*iso*propylfluorophosphate produced, on a number of occasions, not only the quick twitch-like contraction but in addition a secondary, slow development of tension similar to but much smaller than the contracture occurring in denervated muscle. The difference between the normal mammalian muscle and the denervated or the frog muscle is therefore probably quantitative only.

There is one important difference: whereas depression in mammalian muscle by too much acetylcholine is not a physiological phenomenon, contractures in frogs are physiological events which may take place instead of propagated contractions, as is shown below.

There is a problem on which opinions differ. Can the same muscle fibre show the phenomenon of contracture and of propagated contraction? Hunt and Kuffler believe that in frog muscle these two abilities are properties of separate fibres, which are distributed differently in different muscles. For instance, the sartorius contains only muscle fibres which give contraction, the rectus only muscle fibres which give contracture. On the other hand, Brecht and Feneis (1950), in Germany, have examined the effect of acetylcholine on single muscle fibres of different muscles in the frog and obtained apparently both effects in the same muscle fibre (see Figs. 13 and 14). The position may vary in different muscles, but the experiments of Brecht and Feneis seem to show that both effects can be obtained from the same muscle fibre. How does acetylcholine produce the double effect? Does it first depolarize the end-plate region which excites the muscle fibre, and then, when the depolarization spreads to the adjacent part of the fibre, contracture sets in? The record of Fig. 13 could well be explained in this way, particularly because, when we again reduce the action of acetylcholine by D-tubocurarine, the slow contraction disappears first (Fig. 13). D-Tubocurarine, as we shall see, counteracts the depolarizing effect of acetylcholine. On the other hand, in the record of Fig. 14 quick contractions occur during the development of the slow shortening—that is, at a time when we should expect the muscle fibre on either side of the end-plate to be inexcitable. How, then, can the fibre be excited in this condition from a depolarization of the end-plate? There might be a simple explanation. Katz and Kuffler (1941) have shown that a single muscle fibre may have more than one motor end-plate. We can thus imagine that depolarization of the one causes the local contracture, depolarization of the other producing propagated contraction. If this muscle fibre should contain only one end-plate, we may assume that the spreading depolarization at first excites the adjacent part of the fibre before it goes itself into the state of local contracture and electrical inexcitability. At present we must wait for further experiments before a definite answer can be given on this problem.

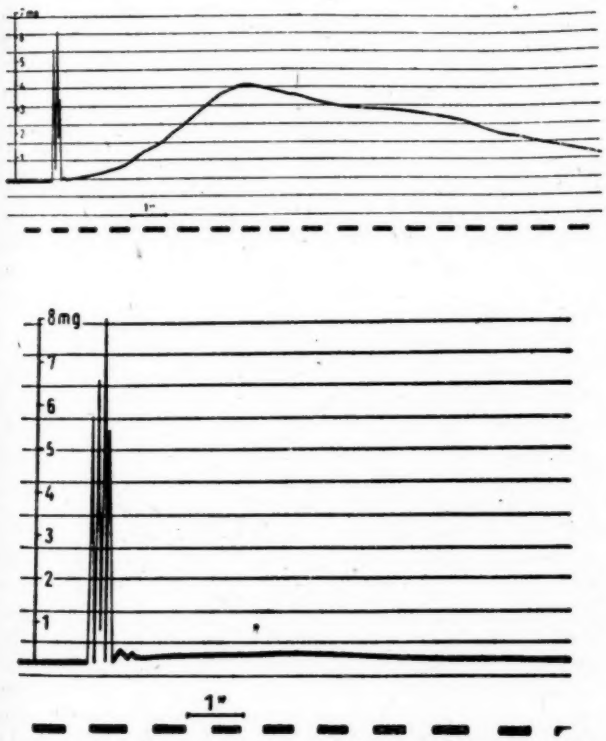

FIG. 13.—Tension record from a single 52-μ-thick muscle fibre of frog's anconaeus muscle (*a*) bathed in acetylcholine 1×10^{-5}; (*b*) effect of acetylcholine 1×10^{-5} for 20 minutes in curare 1×10^{-5}. Ordinates = Tension in mg. Abscissae = Time in seconds. (From Brecht and Feneis, 1950.)

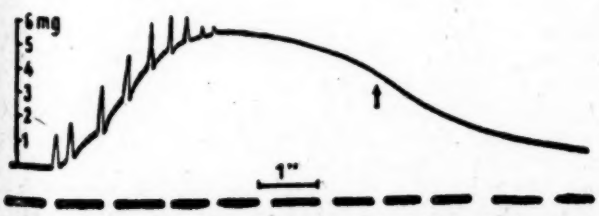

FIG. 14.—Tension record from a single 30–40-μ-thick muscle fibre of frog's anconaeus muscle bathed in acetylcholine 1×10^{-5}. At the arrow, changing bath fluid to Ringer solution. Ordinates = Tension in mg. Abscissae = Time in seconds. (From Brecht and Feneis, 1950.)

Summary of the Action of Acetylcholine

Summarizing, we may say: depolarization of the end-plate by acetylcholine leads to propagated excitation, followed by contraction. If the depolarization of the end-plate, however, spreads to the muscle fibre, two other phenomena may be observed—depression, or contracture; whereas contracture is a physiological event, depression is not. The depression causes neuromuscular block. Thus a substance with acetylcholine-like action can, particularly if it is not quickly destroyed, be an effective neuromuscular blocking agent, and decamethonium—first synthesized by Barlow and Ing (1948) and later by Zaimis (1950b), and introduced as a new curare substitute by Paton and Zaimis (1949)—acts in this way.

Before we discuss neuromuscular transmission, another point is worth mentioning. How are we protected against the action of too much acetylcholine? The distribution of the true cholinesterase, which destroys the released acetylcholine, may give an answer to this question. In a smooth muscle innervated by a parasympathetic nerve, too much release of acetylcholine would have no other action but that of increasing the effect of nerve stimulation. In the skeletal muscle just the opposite effect might be produced, and I think it is for this reason that we find a fundamental difference in the distribution of the true cholinesterase in skeletal muscle and in parasympathetic innervated organs. Here the true cholinesterase is present in the nerve endings, and when the nerve degenerates the true cholinesterase decreases. It is not so with skeletal muscle; here the cholinesterase is also concentrated at the end-plate region. Therefore, no decrease occurs in the true cholinesterase content of muscle after motor-nerve degeneration (Marnay and Nachmansohn, 1937; Couteaux and Nachmansohn, 1938; Feng and Ting, 1938).

3. Neuromuscular Block

In terms of acetylcholine there are three possible ways by which neuromuscular block may be effected: the end-plate becomes less sensitive to the depolarizing action of acetylcholine, or too much acetylcholine is

released so that depolarization spreads beyond the end-plate region, or insufficient amounts of acetylcholine are released by the nerve impulse. All three forms of neuromuscular block have been observed.

D-Tubocurarine

D-Tubocurarine acts by reducing the depolarizing action of acetylcholine, so that the amounts usually released are insufficient to produce this required change at the end-plate. That explains why the anticholinesterases are such good antidotes to curare paralysis.

Decamethonium

In the action of decamethonium we have neuromuscular block produced by too much depolarization, and therefore anticholinesterases would intensify the block. In fact, although it sounds paradoxical, this block could be reduced by D-tubocurarine if given in the appropriate concentration. Recently Burns, Paton, and Dias (1949) have demonstrated the difference of the mechanism in producing neuromuscular block by these two substances on the cat's gracilis muscle. As D-tubocurarine affects only the end-plate, excitation of one nerve-free muscle-end will excite the whole length of the muscle fibre; the excitation will pass beyond the end-plate region, and can be led off from the other end of the muscle. On the other hand, during block produced by decamethonium, the muscle fibre can naturally be excited at the nerve-free ending and the excitation wave will travel along the muscle, but only to the end-plate region; it cannot pass the blocked area—block produced by too much depolarization and no excitation wave will appear on the other side of the motor end-plate.

In the laboratory there is a quick way, without the use of complicated apparatus, to find out if a new neuromuscular blocking agent acts more like D-tubocurarine or more like decamethonium: to test its effect on the frog muscle or on the denervated mammalian muscle. If it acts like decamethonium it will readily cause contracture, but not if it acts like D-tubocurarine, although under certain conditions D-tubocurarine may produce contracture preceding its actual paralysing effect (McIntyre, King, and Dunn, 1945). Decamethonium contractures have been described by Paton and Zaimis (1949) and by Zaimis (1950a).

Botulinum Toxin

The third mechanism—neuromuscular block produced by the inability of the nerve endings to release acetylcholine—is shown in the condition of paralysis produced by botulinum toxin. Guyton and MacDonald (1947) showed that the toxin did not interfere with nerve conduction and that it left the muscle excitable to direct stimulation. Later, Burgen, Dickens, and Zatman (1949) analysed on the rat diaphragm the irreversible neuromuscular block produced by botulinum toxin. The muscle remains excitable to direct stimulation. The nerve still transmits the impulse to the endings. The motor end-plate shows its normal sensitivity to acetylcholine. This was shown by a rather ingenious method of a reversed arterial injection. It is not possible to inject the acetylcholine in such a preparation through the artery, but practically the whole diaphragm drains into a large vein, which empties into the inferior vena cava. They injected the acetylcholine, retrograde, through the vein, and the paralysed diaphragm responded like the normal diaphragm. But when they studied the release of acetylcholine during stimulation they found a greatly reduced output of acetylcholine from the paralysed preparation. The neuromuscular block by botulinum toxin must be explained by an action of the toxin on the myelin-free nerve terminals which prevents release of acetylcholine.

It will be necessary in future to be more cautious in the use of the term curare-like action. This term should be reserved only for neuromuscular block produced by substances which, like D-tubocurarine, have themselves no depolarizing action on the motor end-plate but antagonize those of acetylcholine. If block is not produced in this way, it should be called neuromuscular block, and the mechanism by which it is effected—too much depolarization or too little acetylcholine—should be stated.

4. The Small-motor-nerve-fibre System to Skeletal Muscle

Recently a new problem in neuromuscular physiology has come into the foreground. It concerns the function of the small nerve fibres in motor roots. It has long been known that ventral roots contain, in addition to the well-known large-diameter fibres, a distinct group of small-diameter fibres (Eccles and Sherrington, 1930; O'Leary, Heinbecker, and Bishop, 1934). These have been described in amphibians and mammals, but their function was for a long time unknown. This is no longer so. We may say this fibre system is concerned with the maintenance of long-lasting, sustained contractions, but the mechanism by which these fibres achieve their effect is different in frogs and mammals. We must realize that the same applies to the phenomenon of muscle tone or sustained contractions, which can be brought about by different mechanisms in frogs and in mammals.

The skeletal muscle of amphibia can exhibit slow sustained contractions by its ability to respond to acetylcholine with contracture instead of with propagated summated contractions. The small-motor-nerve-fibre system in frogs is concerned with this form of localized contraction. On the other hand, the normal mammalian muscle, with a few exceptions, does not exhibit this kind of motor response. In mammals "muscle tone" is, as we know since Sherrington (1915) and Liddell and Sherrington (1924, 1925), entirely "reflex tone"; the myotatic reflex is the fundamental basis of postural tone. Myotatic reflexes, however, are practically absent in limb muscles of frogs. The small-motor-nerve discharge in mammals appears to be concerned with regulation of postural reflexes—that is, it acts, as termed by Hunt and Kuffler (1950a), as a muscle proprioceptor regulator. In detail the position in frogs and mammals is as follows.

Experiments on Frogs

The work on the frog is connected with the names of Tasaki and Mizutani (1944), Kuffler and Gerard (1947), Kuffler, Laporte, and Ransmeier (1947). Stimulation of the small motor fibres in frogs sets up local potential changes at the neuromuscular junction which resemble the motor end-plate potential and are called the small-fibre junctional potentials. These do not give rise, like the motor end-plate potentials, to propagated contractions but to localized contractures. But, in order to develop appreciable shortening by this mechanism, the small nerve fibres must be excited repetitively and at a sufficient frequency. Then the small-fibre-junction

potential builds up and a larger and larger part of the muscle fibre becomes involved in the localized contracture.

The small-motor-nerve-fibre system varies in its distribution in different muscles. There are none to the sartorius and adductor longus, but they supply most limb muscles, like gastrocnemius and pectoralis, and some, like the semitendinosus, especially richly. In some muscles the muscle fibres supplied by the small motor fibres form a distinct part—for instance in the ileo-fibularis, where Sommerkamp (1928) spoke of this part as "Tonusbündel." When we assay acetylcholine on the frog rectus abdominis muscle, the assay is made on small-nerve-innervated muscle fibres.

Kuffler, Laporte, and Ransmeier (1947) have shown that there exists in the spinal cord a distinct reflex mechanism, by which the small-motor-nerve-fibre system may be activated exclusively, and that reflexes through this system are widespread in upper and lower extremities. The small nerve fibres can maintain reflexly an appreciable tension, while the twitch system is not, or only slightly, active. The maintenance of long-lasting relatively slow muscle contractions by this mechanism compensates for the absence of myotatic reflexes in the limbs of this species.

Originally Kuffler and Gerard seemed to think that the same muscle fibre might have a double innervation, but recently Hunt and Kuffler (1950b) have expressed the view that the small motor nerve fibres of frog innervate separate muscle fibres from those supplied by the larger nerve fibre group. The observation of Brecht and Feneis that a single muscle fibre shares both responses to acetylcholine makes it necessary to reopen this question. If Hunt and Kuffler are right—and they know more than anyone else about this system—then there is a difference between the frog and a phylogenetically much lower order, Crustacea.

Experiments on Crustacea

In crustacea the same muscle fibre has the stability to exhibit "fast" and "slow" contractions—that is, propagated contractions and localized contractures. In most limb muscles both responses are set up in the same muscle fibre by one and the same nerve fibre, the determining factor being the number and frequency of stimulation (Blaschko, Cattell and Kahn, 1931). But in some muscles—for instance the closer of the claw—the two responses are integrated in a double nerve supply, as in the frog, but here to the same muscle fibre. One motor axon gives rise to large spikes and powerful twitches; the other to smaller end-plate potentials, which on repeated stimulation grow in size and are accompanied by a slow, well-maintained contracture (Pantin, 1936; Wiersma, 1941; Katz and Kuffler, 1946; Kuffler and Katz, 1946).

Experiments on Mammals

In mammals there are also numerous small motor fibres; for instance, about 30% of the efferent myelinated fibres to the muscle of the hind limb in cats are of small diameter. But, as said before, the mammalian muscle does not normally exhibit the phenomenon of local contracture. There have been attempts in the past to find any efferent nerve supply exerting some kind of what was called a tonic function on skeletal muscle. The sympathetic nervous system and a system called the parasympathetic, but transmitted efferently via the posterior roots, has been suggested to have such a function, but it has never been successfully proved.

Häggqvist (1938, 1940) thought that the small motor nerve fibres might exert such a function. He systematically examined the distribution of these fibres in ventral roots of monkeys and further tried to obtain a condition in which the large motor fibres were destroyed. By occlusion of the aorta the cells in the spinal cord are destroyed, and he found that the large anterior horn cells, which give rise to the large-diameter fibres, are more susceptible to ischaemia than the cells of the small-diameter fibre. After 15–20 minutes' ischaemia only the large anterior horn cells were killed. The result was spastic paresis and rigidity. The merit of the experiments of Häggqvist was to draw our attention again to this motor system; but where he erred was to think that the efferent impulses in these fibres produce directly some kind of tonic effect on the muscle.

A clear insight of the functions of these fibres in mammals was given by Leksell (1945). He examined the effect of stimulating the small motor fibres without stimulating the large ones. For that purpose he eliminated conduction in the large fibres by applying a pressure block or a polarization block to the nerve trunk. For instance, an effective selective pressure block could be achieved by a simple spring clamp, padded with soft rubber cushions and tightened with a screw. The nerve was then stimulated proximal to the site of compression and only small fibres were found to conduct beyond the block.

These impulses did not produce contraction of the innervated muscle, but they had a very definite effect on the afferent discharge from the muscle proprioceptors. Provided that the muscle was under a certain stretch, stimulation of the small motor fibres considerably increased the discharge of the afferent nerves, and he definitely stated that these small motor fibres served as regulators of sensory activity originating in the muscle.

The problem has recently been taken up by Hunt and Kuffler (1950a, 1950b). They could confirm Leksell's statement that no detectable contractile response or propagated muscle impulse was produced. But these small motor nerve fibres, when excited, set up local potentials apparently arising from the muscle elements within the muscle spindles, the intrafusal muscle fibres, and this apparently increased the discharge in the afferent nerve fibres. They used an extremely elegant method—a preparation consisting of a single small efferent fibre, the components of a muscle spindle, and a single afferent fibre. Stimulation of the small nerve fibre would cause a discharge in a receptor which had been quiescent, or could increase an existing discharge rate. The effect was influenced by existing muscle stretch being increased at higher muscle tension. This is not a new conception, for Matthews in 1933, in his classical studies on nerve endings in muscle, had already stated quite clearly that the intrafusal fibres are contracted by impulses travelling down the small motor nerve fibres, and that the sensory endings in the spindle are then stimulated by the mechanical effect of the contraction.

We know the intrafusal muscle fibres have motor end-plates: no experiments have as yet been performed to show that they are depolarized by acetylcholine, or, in other words, that the small-motor-fibre system is cholinergic. It is unlikely, however, that it should be otherwise. On the assumption that all motor fibres in the ventral roots are cholinergic, there still remains this difference: whereas with the large motor system and

with the small motor system in frogs the contractile effect upon the muscle fibre is the final event, with the small motor system in mammals this is not so. Here the contraction presents an intermediary stage; it acts as a mechanical stimulus for exciting the nerve endings in the spindle and thus sets up an afferent discharge. We shall probably hear much more about this system in the future.

It may be felt that when discussing the small-motor-fibre system I should have confined myself to mammalian muscle. But we are not certain whether the more primitive mechanism of producing sustained contraction in frogs and crustacea may not exist in some mammalian muscle—for instance, in the eye muscle. Further, under abnormal conditions—for instance, after denervation—the mammalian skeletal muscle reverts to the more primitive form of response; that is, localized contracture. This phenomenon is understandable only under the wider phylogenetical aspect. But the main reason is that I found it so fascinating to see how Nature ingeniously adapts parts of an old system, the small-motor-fibre system, to a more complicated mechanism in the development of postural reflexes in higher animals, that I could not resist giving the full story so far as it has been unravelled by recent experiments.

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EOSINOPHIL AND OTHER LEUCOCYTE CHANGES IN BURNED PATIENTS

WITH SPECIAL REFERENCE TO ADRENO-CORTICAL ACTIVITY

BY

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An injection of anterior corticotrophic hormone of the hypophysis (A.C.T.H.) produces a marked fall in the eosinophils in the blood, associated with lymphocytopenia and neutrophil leucocytosis: in patients with Addison's disease, however, cortisone, but not A.C.T.H., produces similar effects (Thorn *et al.*, 1947a; Dougherty and White, 1947; Forsham *et al.*, 1948; Hills *et al.*, 1948; Prunty, 1950). The leucocyte changes, therefore, are mediated through adrenocortical stimulation by the anterior pituitary. Selye (1950) maintains that the major endocrine response to stress is an increased secretion of A.C.T.H. by the pituitary, which induces glyco-corticoid secretion by the adrenal cortex. The cortical hormones act on the peripheral organs and produce eosinopenia, lymphocytopenia, and neutrophilia.

The initial polymorphonuclear leucocytosis in burned patients is well known (Locke, 1902; Dorrance, 1933; McIver, 1933; Brown, 1944), and reference has been made to eosinopenia (Schreiner and Pucsko, 1925; Crassweller *et al.*, 1950a). The purpose of this study was to follow the changes in number of the blood leucocytes of recently burned patients and to correlate the findings with the extent of burning and other factors. In this way it was hoped to gain information on adrenocortical activity.

The Burned Patients

Thirty-five patients (19 males, 16 female) were studied; they were all between the ages of 13 months and 80 years and the extent of burning varied from 0.1% to 80% of the body area (Table I). Twenty-seven were admitted to the Burns Research Unit within three hours of burning, most within an hour or two, and all within nine hours. Twenty-four were or became clinically shocked and 26 were transfused with plasma or dextran or both fluids.

Eight patients died—two were moribund on admission and died a few hours later, five died two to four days

TABLE I.—*The Burned Patients*

Case No.	Sex and Age (Years)	Clinical Shock	Body Area Burned	Sites of Burning	Lived or Died and Day of Death
1	M 18/12	−	0·1%	Left hand	Lived
2	M 33	−	4%	Small metal burns face, neck, right arm, and back	,,
3	M 25	−	4%	Both hands and arms	,,
4	M 15	−	5%	Face, hand	,,
5	M 4	−	7%	Scald right leg	,,
6	M 13	+	9%	Back, right arm, shoulder, axilla	,,
7	M 35	−	8%	Face, both hands, wrists	,,
8	F 2	∓	9%	Back	,,
9	F 2½	−	7%	Back	,,
10	M 13/12	±	10%	Scald left chest, left hand	,,
11	M 50	∓	11%	Face, chest, arms, thighs	,,
12	F 4	±	11%	Right arm, right thigh, chest	,,
13	M 23	+	12%	Face, neck, upper chest, hands	,,
14	F 4	±	13%	Right upper chest, axilla, face, thighs	,,
15	M 2	+	15%	Lower face, chest, upper abdomen, front thighs	,,
16	F 55	+	17%	Scalds legs	,,
17	F 3	+	18%	Abdomen, back, thighs, left arm, right hand	,,
18	F 2	+	20%	Back of chest to buttocks	,,
19	F 68	+	22%	Scalds left upper arm, left side of trunk and buttock	,,
20	M 28	+	25%	Face, arms, chest, back	,,
21	F 2½	+	25%	Scalds back, buttocks, leg, flank, left arm	,,
22	M 38	++	26%	Right arm, left forearm, hand, face, scalp, right leg	,,
23	M 20	++	30%	Face, neck, chest, arms	Died, 2
24	F 13	+	30%	Half lower back, buttocks, thighs, and inside right forearm	,,
25	M 4	+	30%	Chin, neck, chest, abdomen, upper thighs	Lived
26	F 58	++	35%	Abdomen, buttocks, perineum, thighs, left arm	Died, 3
27	F 3	+	36%	Abdomen, buttocks, thighs, arms	Lived
28	M 80	++	40%	Buttocks, lower abdomen, thighs, scrotum, upper legs	Died, 0
29	F 9	++	42%	Face, neck, arms, trunk, thighs	Died, 2
30	F 5½	++	47%	Arms, trunk, thighs	Lived
31	F 8	+	47%	Front chest, abdomen, buttocks, thighs, hands	,,
32	M 36	++	50%	Face, trunk, arms, forearms	Died, 9
33	M 27	+	65%	Face, neck, both arms, hands, chest, back, right thigh	Lived
34	F 5	++	75%	Whole trunk, neck, arms, thighs, legs	Died, 2
35	M 22	++	80%	Entire body except feet and lower legs	Died, 0

0 = Day of burning; 1, 2, etc., following days.
Shock: − absent, ∓ doubtful, ± slight, + definite, ++ severe.

after burning, and the other on the ninth day. Twenty-one patients were discharged with healed or successfully grafted burns 1 to 15 weeks after admission, and at the time of writing the remainder have been in hospital 2 to 12 weeks and are doing well.

A patient with, say, 10% of his body surface burned is referred to as a 10% burn. In certain analyses the patients are grouped into 0–10%, 11–20%, 21–30%, and more than 30% burns.

Outline of Treatment.—At the initial dressing 1% cetrimide was used to clean the skin and then penicillin cream, often supplemented by polymyxin cream, was applied. Local sulphonamides were not used. This was fortunate, as Brown (1944) found that sulphonamide cream depressed the leucocyte count. In the non-shocked patients skin-grafting of deep burns was generally carried out on the first or second day. Shock was combated by intravenous plasma or 6% dextran in saline, or both, and repeated haematocrit observations were made. Sometimes blood transfusions were given. In shocked patients skin excision and grafting was delayed for a week or longer. Blood transfusion was given for anaemia and during most of the operative procedures. Diet was of the high-calorie high-protein type.

Methods

Blood counts were from ear or finger-prick blood, the first drop being discarded. Differential counts were made from Leishman-stained films on slides, and at least 400 leucocytes, often 600 to 1,000, were enumerated. In this paper the neutrophil polymorphs, metamyelocytes, and myelocytes are grouped as neutrophil cells.

Eosinophil counts were carried out by the direct "wet-field" method of Dunger (1910). Every few days the diluting fluid, consisting of 1 ml. of 1% aqueous eosin Y, 1 ml. of acetone, and 18 ml. of distilled water, was freshly prepared, and each day it was filtered. Blood was diluted 1 in 20 with this fluid in each of two white-cell pipettes: within a few minutes a double-sided Fuchs–Rosenthal chamber was filled from each pipette and the eosinophils in four entire fields were counted. The volume of the blood containing these cells was 0.65 c.mm. A number of parallel counts by both Dunger's (1910) and Randolph's (1949) methods gave very close results.

In the first 18 cases the counts were usually performed twice daily during the first three to five days after burning, daily for the next week, and thereafter every two to four days until discharge. The general pattern of leucocyte changes had by then been established. Only eosinophil counts which were regarded as of special interest were carried out on the next 17 patients. They were usually performed four times a day during the period of eosinopenia and at the beginning of the post-eosinopenic rise (see below), twice daily during the next few days, and thereafter less often.

In 16 patients several eosinophil counts were made at about hourly intervals for three to six hours on the day of admission. The first counts were performed on 11 patients within two hours of burning, on 11 others within the third hour, and on all within 24 hours.

TABLE II.—*The Eosinophil Counts per c.mm. of Blood in 19 Patients, Showing the Development of Eosinopenia After Burning*

Case No.	Hours after Burning								
	1–	2–	3–	4–	5–	6–	7–	8–9	18–30
1		68	40	28	19				9, 31
5	1,270		276	87					42, 192
7	177	100	26	18	9	21			47, 90
9		716	767	450	165			99	31, 87
11		50	19						0, 0, 0, 0
12		53	11	5		0			0, 3, 2, 7
14		304		32		6			0, 0
15	6						0		3
16	74 31	25	3	0					0, 0
17		29	8	0					0, 6, 4, 4
18				11	5	0			0, 0, 0
20	20		0						0, 0, 0
21	281	212	56					6	0, 3
25	13								0, 3
26	19	14	3	0					0, 0, 0, 0
28	257	276	268*						
32		19	34		0		0		0, 0
33	170		36	11		9			20, 3, 8, 11
35		174	71	55	*				

* = Time of death.

Normal Eosinophil Values.—In our experience the eosinophil level in normal subjects usually varies between 100 and 300 per c.mm. and may fluctuate during the day and from day to day. In this paper the lowest normal level is accepted as 40 per c.mm. Values up to 400 are not considered to indicate eosinophilia.

Eosinophils (Figs. 1 to 6)

The changes in the eosinophil count after burning followed a constant pattern. Within a few hours of burning the number of circulating eosinophils was found either to be falling or to have fallen to low or zero values. The eosinopenia was maintained for a variable number of days, after which the count began to rise. Later a peak value was reached, and then the eosinophil count declined. The pattern was therefore one of *post-burn fall, period of eosinopenia, post-eosinopenic rise, and later changes.*

The Post-burn Fall

In 10 patients on whom eosinophil counts were repeated hourly or so on the day of admission, the eosinophils fell progressively from normal or supra-normal values to reach low or zero levels a few hours later (Table II). The hourly changes in Case 7 are shown graphically in Fig. 1. In nine other patients the eosinophil levels were already low within a few hours of burning and sometimes a fall from a low to a lower level was found—for example, Cases 17 and 26.

As the eosinophil counts before burning were unknown, it was impossible (except in Case 9) to determine how soon the fall began. However, the interval between burning and the onset of a definite fall in the eosinophil count was determined in 18 patients, and was found to be within two hours in seven and within four hours in the remainder. The interval between burning and the onset of eosinopenia (defined as less than 40 cells per c.mm.) was determined in 19 patients and found to be within two hours in five, between two and four hours in eight, and after four hours in the remainder.

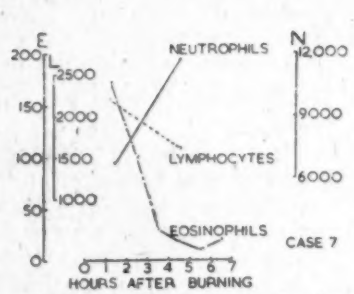

FIG. 1.—Serial counts on the day of burning. As the eosinophils fall to reach an eosinopenic level there is a moderate lymphocytopenia and a definite neutrophil leucocytosis (Case 7).

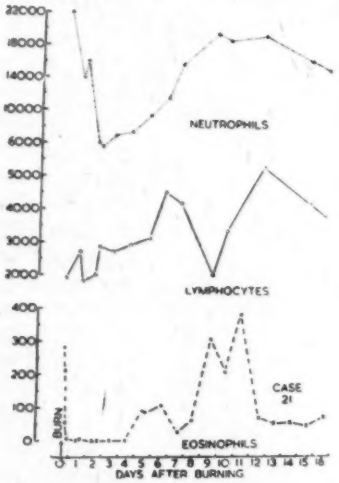

FIG. 3.—Serial neutrophil, lymphocyte, and eosinophil counts in Case 21.

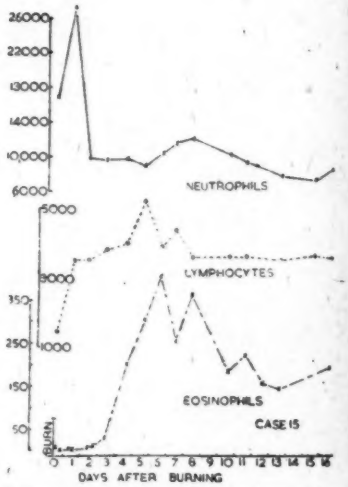

FIG. 4.—Serial neutrophil, lymphocyte, and eosinophil counts in Case 15.

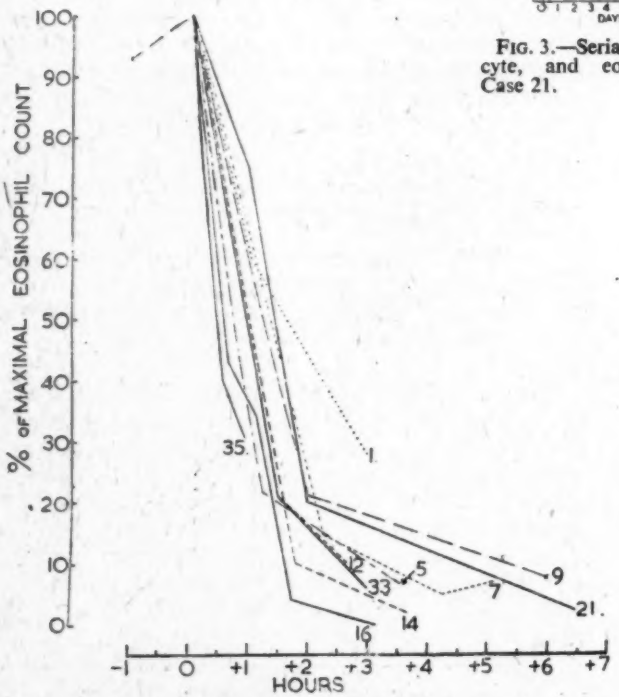

FIG. 2.—The curves show the rates of disappearance of the eosinophil cells after burning in ten patients. The 100% values are the maximum values found and are plotted at zero hour. The curves of the extensively burned shocked patients are the non-interrupted heavier lines. There is no gross difference in the rates of disappearance of the eosinophils from the blood in the different patients. Beyond about +2 hours the curves flatten to the right and represent the established eosinopenic state rather than a slowing down of cell disappearance. Note that the numerals in this and all subsequent figures refer to case numbers.

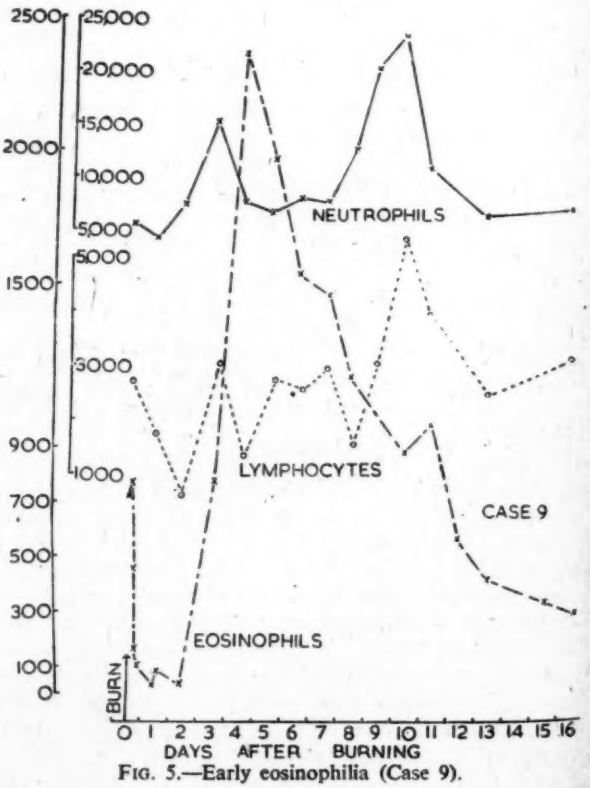

FIG. 5.—Early eosinophilia (Case 9).

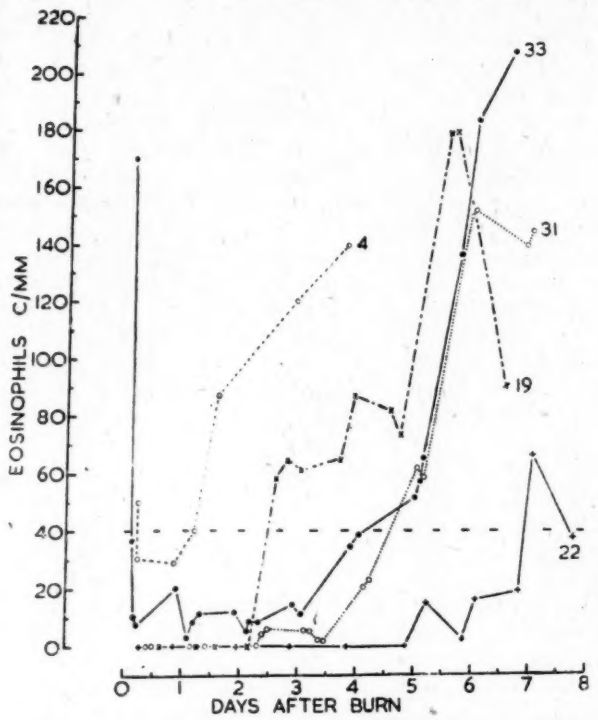

FIG. 6.—Serial eosinophil counts during the first week after burning in five patients. The falling of the eosinophil count soon after burning is seen in Case 33 and then a period of eosinopenia occurs, present in all the cases. This lasts from one to seven days and is followed by a rise in the count. Below the horizontal interrupted line at 40 eosinophils per c.mm. the counts are considered eosinopenic. Note that the end of the eosinopenic stage is sometimes heralded by a small rise in the count for one or two days (Case 22).

The *rates* of disappearance of the eosinophils from the blood in 10 patients are shown in Fig. 2; the steepness of the curves gives the rates of eosinophil disappearance. Similar rates of eosinophil disappearance occurred both in the extensively burned shocked patients (heavier non-interrupted curves) and in the less-burned non-shocked patients. The rates of disappearance vary between 30% and 70% of the cells an hour.

Period of Eosinopenia

It has been shown that a rapid disappearance of eosinophils occurs within a few hours of burning and an eosinopenic state with very low or zero levels is soon established. The eosinopenia is maintained for varying periods in different patients.

The duration of eosinopenia was defined as the interval between the time of burning and the time at which the eosinophil count first reached a level of 40 per c.mm. during the post-eosinopenic rise. The latter point was often interpolated from the curve. The *true* period of eosinopenia was some hours shorter than this and the error of the calculations was within $\pm\frac{1}{2}$ day.

In 28 patients surviving this period (including two who subsequently died and another recent case not included in Table I), the duration of eosinopenia was plotted against the percentage area burned (Fig. 7). The mean periods in groups of these patients are shown in Table III (p. 982). The eosinopenia lasts about one to two days in patients with burns less than 10% in extent (mean, 1.3 days), and is longer, usually three to five days (mean, 4.0 days), in those more extensively burned. This is statistically significant, but the

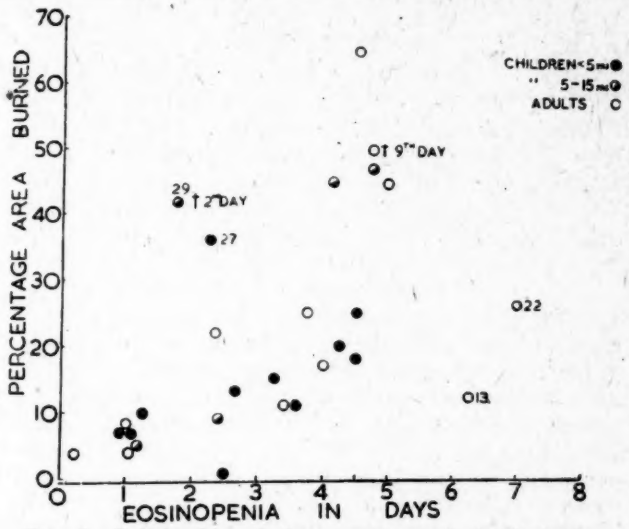

FIG. 7.—Relationship of the percentage of the body area burned to the duration of eosinopenia in 28 patients (see text). † = Died.

relationship between the two variables—duration of eosinopenia and percentage area burned—is not a simple direct one. In Fig. 7 it appears to be an exponential curve, with its concavity facing to the left, rising steeply between four and six days after burning. A few points fall away from the curve, and their significance is discussed later.

Post-eosinopenic Rise (Figs. 3 to 6)

The end of eosinopenia was often heralded by a slight increase in the count, but often this was abrupt. The eosinophil concentration progressed for several days to reach a peak: sometimes the rising curve was interrupted by one or two temporary falls, occasionally to an eosinopenic level, and then rose again to a greater height (Fig. 3).

The heights of the peaks varied considerably; in 13 patients they were between 70 and 250 cells per c.mm., and in eight others values between 350 and 500 were found. Such temporary high borderline values cannot be regarded as a true eosinophilia, but are probably due to the rebound phenomenon often found when retardation is succeeded by a relative absence of restraint.

However, in four patients abnormally high levels were found, termed "early" eosinophilia.

Early Eosinophilia in Burns (Fig. 5)

In two children (Cases 5 and 9) an eosinophilia preceded the fall to eosinopenia (Table II), and the post-eosinopenic rise was exaggerated into what may be termed an acute attack of eosinophilia, which also occurred in two other children (Cases 8 and 14). The maximum counts were 693, 981, 2,360, and 1,875 (5%, 8%, 23%, and 20% of the total leucocyte counts), and the eosinophilia lasted 6, 10, more than 14, and 8 days respectively.

In Case 5 an acute otitis media was diagnosed the day before the onset of the post-eosinopenic eosinophilia. In Case 9 (Fig. 5) the onset of this eosinophilia coincided with a generalized erythema sparing the face, a pyrexia of 104° F. (40° C.), and a one-day neutrophil peak of 15,000 per c.mm.; group A haemolytic streptococci were isolated from the throat and burned skin. No intercurrent infection was noted in the other children.

Later Eosinophil Changes

After the peak rise the eosinophil level usually declined, but remained within normal limits. In some severely burned patients the eosinophil count remained low for two to four weeks as if adrenocortical hyperactivity was continuing (see below). In many patients sudden but temporary falls in the eosinophil level occurred, often related to a surgical operation or to infection.

Late Eosinophilia in Burns

In five patients eosinophilia occurred four to six weeks after burning. In Case 5 early eosinophilia was found, but during the next five and a half weeks the eosinophils did not exceed 350 per c.mm. However, the count rose to 484 per c.mm. on the 40th day, was 840 five days later, 1,431 on the 49th day, forming 11% of the total white cell count, and before discharge on the 52nd day was 1,256 per c.mm. In Case 14 early eosinophilia occurred, after which the eosinophil count subsided, and then on the 27th and 30th days values of 601 and 606 per c.mm. were found. Case 13 did not have eosinophilia until the 40th day, when the count was 710 per c.mm. (6% of total leucocytes), and the eosinophilia persisted, with maximum counts of 1,100 per c.mm. on the 47th and the 48th days, until the 56th day, after which the level fell to normal. In Case 19 eosinophilia began on the 33rd day, when the level was 500 per c.mm., and this continued for 12 days. In Case 27 eosinophilia began on the 43rd day, when the count was 580 per c.mm., and persisted for about a week.

Twenty patients remained in hospital longer than 21 days, and 15 more than 28 days. As this eosinophilia is delayed until four to six weeks after burning, its true incidence was 5 out of 15 or 20 patients (25 or 33%).

We do not know the aetiology of late eosinophilia, but it may be due to sensitization to a drug used in treatment.

Lymphocytes

In six patients two or more lymphocyte counts within a few hours of burning were performed, and two children showed a marked fall from high levels. For example, in Case 5 the count of 9,700 per c.mm. at one and one-quarter hours after burning fell to 4,500 and 2,500 at two and three hours. In three patients a smaller fall was observed—for example, Case 7 (Fig. 1). In other patients low lymphocyte counts during the first day or two were followed by higher counts on succeeding days (Figs. 3 and 4), suggesting that an early lymphopenia was present.

Therefore, a lymphopenia commonly occurs after burning; it may be marked in some children, but is usually moderate and lasts only a day or two. Subsequently, the lymphocyte level varied considerably: a lymphocytosis sometimes accompanied the post-eosinopenic rise or the secondary neutrophil wave.

Neutrophils

The Primary Neutrophil Wave (Figs. 1, 3, 4, and 5).—It is well known that a neutrophilia follows burning (Locke, 1902; McIver, 1933; Brown, 1944); in this study this was confirmed and is called the *primary* neutrophil wave. The onset of the leucocytosis was rapid; commonly the count was high within a few hours of burning and was always at its maximum within 24 hours, often within the first few hours. Then the count fell, usually rapidly at first, to normal levels on the second to the fourth day, so that the primary wave lasted from one to three days. In three patients, for example Case 15 (see Fig. 4), the count fell, but remained high for four to six days after burning, rising again as the secondary neutrophil wave set in. The height of the primary wave was related to the extent of the burning—for example, in five of the eight patients with less than 10% burns the maximum counts were between 10,000 and 15,000 per c.mm., and in eight of the ten more extensively burned patients studied the maxima were more than 20,000 per c.mm. The highest counts recorded, which never exceeded 40,000 per c.mm., all occurred in severely shocked patients. Primary neutrophilia did not occur in two patients with burns less than 10% in extent (Case 6; Case 9, Fig. 5).

The Secondary Neutrophil Wave (Figs. 3, 4, and 5).—In 13 of the 16 patients investigated a definite or marked increase in the neutrophil count began five to ten days after burning even if a primary wave did not occur (Fig. 5). The count increased to a maximum and then declined to a normal level two to fourteen (usually three to eight) days later. This leucocytosis did not occur in three of the eight patients with less than 10% burns; in four others the maximum counts were below 13,000 per c.mm. The secondary waves were usually higher in the more extensively burned in whom they were always found, and the maximum counts were usually more than 15,000 per c.mm. The secondary rise of leucocytes has been observed by Brown (1944), who considered that it was probably due to infection of the raw burned surfaces. The bacteriology of the burned skin in our series throws no light on this.

Discussion

Eosinopenia and Adrenocortical Hyperactivity in Burns

Among the effects of A.C.T.H. and 11-oxysteroids is a fall in the eosinophil count associated with a degree of lymphocytopenia and neutrophil leucocytosis (Thorn *et al.*, 1947a; Dougherty and White, 1947; Hills *et al.*, 1948; Forsham *et al.*, 1948). The same blood changes taking place after burning suggest that adrenocortical hyperactivity occurs in the burned patient, and the association of a more prolonged eosinopenia with more extensive burns suggests that the hyperactivity is more prolonged in these patients.

Other evidence supports this contention. Many of the effects of burning resemble those of administration of A.C.T.H. or adrenal steroids. Sodium and chloride retention and increased potassium loss occur both during the first few days after burning (Moore *et al.*, 1950) and after injection of A.C.T.H. or deoxycortone (Prunty *et al.*, 1948; Forsham *et al.*, 1948): similar disturbances of carbohydrate metabolism, including hyperglycaemia, sometimes glycosuria, and lactic acid acidaemia, occur in experimental burns (Clark and Rossiter, 1944), human burns (Taylor *et al.*, 1944), and after the administration of A.C.T.H. or cortisone (Forsham *et al.*, 1948; Conn *et al.*, 1949; Sprague *et al.*, 1950), and the hyperglycaemia in rats after burning can be prevented by previous adrenalectomy (Clark and Rossiter, 1944).

Similar changes in nitrogen metabolism, such as increased nitrogen excretion, follow burns (Cope *et al.*, 1943; Levenson *et al.*, 1945; Keyser, 1948; Moore *et al.*, 1950) and occur after the administration of A.C.T.H. and 11-oxysteroids (Long *et al.*, 1940; Sprague *et al.*, 1950). Degenerative changes in lymphoid tissue occur after burning (Bardeen, 1898; Baker, 1945) and after injection of A.C.T.H. (Dougherty and White, 1947).

There is an increase of the urinary excretion of 17-ketosteroids (Cope *et al.*, 1943) and of biologically active reducing glyco-corticoids (Heard *et al.*, 1946) after burning and after injection of A.C.T.H. in the intact animal or man (Thorn *et al.*, 1947b; Venning *et al.*, 1948; Prunty, 1950; Sprague *et al.*, 1950). The ascorbic acid content of the adrenals in the rat (Clark and Rossiter, 1944) and of the blood in man (Abbott *et al.*, 1946) falls after burning, and a similar adrenal depletion occurs after the administration of A.C.T.H. (Long, 1947; Sayers and Sayers, 1949). Again, the cholesterol content of the adrenal in rats is decreased both after burning and after A.C.T.H. (Long, 1947).

We may therefore conclude that the adrenal cortex is actively stimulated in burns through an increased production of A.C.T.H. by the pituitary.

Hypothalamic Control.—De Groot and Harris (1950) have shown that the adrenocorticotrophic secretion of the anterior pituitary in rabbits is under hypothalamic control, and Hume and Wittenstein (1950) draw a similar conclusion from their work in dogs. Hume and Wittenstein also showed that the hypothalamus can be activated by nervous impulses from an injured area, and this is obviously of significance in burns.

Adrenocortical Failure in Burns

We may therefore infer that if a lesion develops in the hypothalamus, pituitary, or adrenal it may have the same effect on adrenocortical activity—that is, the adrenal cortex may fail to function. The term "adrenocortical failure," which will henceforth be used in a functional sense, does not *necessarily* imply that the fault lies in the adrenal itself, although this may be so.

It is important, therefore, to determine whether adrenocortical failure occurs and can be diagnosed in some burned patients, as "replacement" therapy with A.C.T.H. or cortisone may then be indicated.

The Eosinophil Changes in Fatally Burned Patients (Fig. 8)

If acute adrenocortical failure occurs in some burned patients its incidence is probably greater among those who later succumb than among those who survive. An analysis of the eosinophil changes in eight fatal cases was therefore made with this in mind.

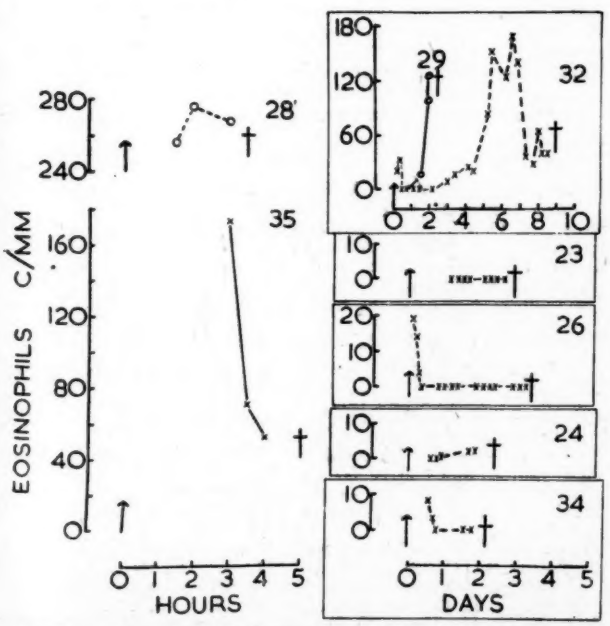

FIG. 8.—The eosinophil changes in eight fatally burned patients. The arrows indicate time of burning, the daggers times of death. Hours (or days)=hours (or days) after burning.

One of these patients died four hours after burning while the eosinophil count was falling, and four others died two to three days after burning during the established period of eosinopenia. Such changes, we believe, are due to hyperactivity of the adrenal cortex. In the remaining patients the possibility of adrenocortical failure arose.

In Case 28 the eosinophil counts 1½, 2, and 2½ hours after burning were 257, 276, and 268 per c.mm. respectively, and the patient died 15 minutes after the last count. The failure of the count to fall does not exclude the possibility that eosinopenia may have occurred later had he lived long enough. In support of this, the post-mortem histology revealed large numbers of eosinophils in the spleen and moderate numbers in other organs. This may indicate the removal of eosinophils from the peripheral blood, as similar changes have been noted in other patients dying within 24 hours of burning (unpublished observations). On the other hand, the patient presented some evidence of Cushing's syndrome—namely, obesity, bilateral lipoid-laden, hypertrophic, and convoluted adrenal cortices (together both glands weighed 30 g.), a pituitary in which the basophils were numerous and eosinophils few in number, a cystic thyroid, a fatty liver, and sclerosis of the vessels of the liver, kidney, and other organs. In this patient, therefore, the burning may have been unable to produce the normal response from the abnormal pituitary and adrenal glands, but the evidence was inconclusive.

In Case 29 the eosinophil count was zero at 12 and 14 hours after burning, suggesting early hyperactivity of the adrenal cortex. Shock and haemoconcentration were treated with 6 litres of dextran and 0.5 litre of blood. A transient haemoglobinuria was noted three hours after burning, and oliguria developed at nine hours. At 30 hours the patient's temperature suddenly increased to 104° F. (40° C.), pulse 120, and respirations 50. At 38 hours the eosinophil count was 11 per c.mm., and two hours later this had risen to 99. The eosinopenic period lasted therefore only one and two-thirds days. From Fig. 7 a period of four to five days with this extent of burning would have been expected—that is, a "premature" rise in the eosinophils took place. At this time the patient was very ill, her respirations were still 50 a minute, she was very restless, and her extremities were cold: two hours later she died suddenly, and the possibility of acute adrenocortical failure arose, possibly due to hypothalamic changes.

Unfortunately permission for a necropsy was refused, but blood removed from the heart 30 minutes after death gave a count of 127 eosinophils per c.mm. and confirmed the "premature" post-eosinopenic rise. In addition, the lymphocyte count was 4,700 per c.mm. (total leucocytes, 18,000 per c.mm., neutrophils, 71%), and in support of adrenocortical failure was a relatively low blood glucose of 80 mg. per 100 ml. The relatively low plasma sodium of 300 mg. per 100 ml. and very high plasma potassium of 36 mg. per 100 ml. (the plasma was separated soon after collection of the blood and showed no visible haemolysis) could support such a diagnosis, but the oliguria complicated the problem.

In the eighth case (Case 32) eosinopenia was established within two hours of burning, lasted four and a half to five days, when the rise in blood eosinophils

occurred, and the patient died on the ninth day. From an analysis of the clinical symptoms, blood changes, and post-mortem findings the evidence for adrenocortical failure was inconclusive.

Therefore the eosinophil changes in five out of eight fatal cases suggested that hyperactivity of the adrenal cortex was present before death: in another patient there was evidence suggesting that adrenocortical failure had occurred, and in two others the evidence was inconclusive.

Steroid Therapy in Burns

Deoxycortone acetate and extracts of the adrenal cortex have been used therapeutically in burns (Wilson *et al.*, 1936, 1938; Einhauser, 1939; Elkinton, 1939; Ivory, 1940; Scudder, 1940; Cope *et al.*, 1943; Rhoads *et al.*, 1943), but the results reported by different workers are not consistent. Beneficial results have been claimed but are often difficult to evaluate and sometimes not impressive; nevertheless some dramatic recoveries have been reported. However, the purified glyco-corticoid hormones of the adrenal were not then available. More recently Crassweller *et al.* (1950b) supplemented the treatment of three burned patients with cortisone. Two died and the survival of the third may or may not be related to the use of cortisone. Crassweller and his colleagues (1950a) claimed to have lowered the death rate from a standard experimental burn in mice by treatment with a special extract of normal urine prepared in such a way that it was likely to contain cortisone. Their results, which are suggestive, are not, however, conclusive, as certain experimental precautions, notably the control of environmental temperature, were not taken.

Hyperactivity and Failure of Adrenal Cortex and the Period of Eosinopenia

I have shown that eosinopenia develops after burning and have produced evidence which indicates that this is a sensitive reflection of adrenocortical hyperactivity; furthermore, I have found that the duration of eosinopenia is related to the percentage area burned (Table III).

TABLE III.—*A Comparison of the Mean Durations of Eosinopenia in Groups of Patients with Burns of Different Extent*

	Body Area Burned				
	0–10%	11–20%	21–30%	>30%	>11%
No. of patients ..	9	8	4	7	19
Mean duration of eosinopenia in days ..	1·3	4·0	4·4	3·8	4·0
Standard deviation ..	0·66	0·95	1·7	1·3	0·98

A statistical comparison of the mean durations of eosinopenia in the 0–10% and >11% groups shows a highly significant difference ($t = 5{\cdot}712$, $p < 0{\cdot}001$).

In Fig. 7 the points of four patients (Cases 13, 22, 27, 29) fall well to the right or well above the correlation zone, and the question arises whether these variations are within "normal limits" or if they represent departures from the normal. In Case 13 (12% burn) the burn shock was greater than was expected from the extent of burning; in Case 22 (26% burn) the area burned did not reflect either the severity of burning (one limb was charred and had to be amputated) or the severe degree of clinical shock. If the period of eosinopenia measures the duration of the adrenocortical reaction to burn stress, and the percentage area burned is merely an index of the stress present, then the "prolonged" eosinopenic periods in these two patients can be accounted for. Similarly in Case 27 (36% burn) burn shock was present, but was not severe and was easily controlled. On the other hand, if the period of eosinopenia is appreciably shorter than that expected from the area burned—i.e., if a "premature" post-eosinopenic rise in the eosinophils occurs—adrenocortical failure may be suspected, particularly if the patient is at the same time seriously ill. Case 29 was such a patient.

Summary

The quantitative changes in the eosinophil counts in 35 patients, and of the lymphocyte and neutrophil counts in 18 patients, with burns of various degrees of severity have been studied. Soon after burning, the eosinophil count falls and reaches low or zero values in a few hours; this is often accompanied by a lymphocytopenia and usually by a neutrophil leucocytosis (primary wave).

The eosinopenia, which may persist for a few days, lasts longer in the more extensively burned patients. In four patients an early eosinophilia was found, and in two it was associated with intercurrent infection. In five patients a delayed eosinophilia began four to six weeks after burning.

The height of the primary neutrophil leucocytosis generally increases with the percentage area burned. A further neutrophil leucocytosis (secondary wave) develops five to ten days after burning.

The significance of eosinopenia in burns is discussed in the light of the known biological and metabolic effects of burning and of the recent knowledge of A.C.T.H. and cortisone. It is suggested that the eosinopenia is a sensitive index of adrenocortical activity in burns.

The possibility that adrenocortical failure may occur in some burned patients is raised, and it is suggested that a "premature" rise in the eosinophil count in relationship to the percentage area burned may help in such a diagnosis.

The eosinophil changes in five out of eight fatally burned patients suggested that in them hyperactivity of the adrenal cortex was present before death. In one other there was some evidence for adrenocortical failure.

This work has been carried out in the M.R.C. Burns Research Unit, Birmingham Accident Hospital, with a part-time grant from the Medical Research Council which is gladly acknowledged. Thanks are due to Mrs. J. Napthine and Mr. R. Vince, who did most of the leucocyte counts; to the surgical and nursing staff of the Burns Unit for their co-operation, in particular to Sister M. Nicholls and to Mr. Douglas Jackson; to my secretary, Miss M. Hayes; to my senior technical assistant, Mr. L. Nelson, who drew most of the figures; to Messrs. R. Gill and C. Richardson, who photographed them, and to various other colleagues and members of the laboratory staff.

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SOME OBSERVATIONS ON SURVIVAL OF PATHOGENIC BACTERIA ON COTTON-WOOL SWABS

DEVELOPMENT OF A NEW TYPE OF SWAB

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This inquiry was prompted by our doubts on the reliability of culturing swabs when examination had been delayed by sending the specimens through the post or by depositing them after laboratory hours. Our laboratory is often obliged to carry out such delayed examinations, but similar delays must be fairly common in hospital and public health bacteriology. Apart from a few isolated statements, little attention has been given to the question of survival of the common pathogenic organisms on cotton-wool swabs.

The earliest account describing the use of cotton-wool swabs in clinical pathology appears to have been given by Councilman (1893), who recommended their employment in the bacteriological diagnosis of diphtheria. About this time Continental and English workers were using a variety of bizarre methods. For example, in France, Roux and Yersin (1890) described the use of a platinum wire flattened at the end for sampling from diphtheritic membranes. Goldscheider (1893), in Germany, used a platinum scoop; Hamilton (1895), working in London, suggested a goat's-hair brush; Hardman (1895) preferred to collect the discharges on a white paper which could then be dried before a fire and sent to the laboratory by post. Preston (1896) and Hewlett and Nolan (1896) were among the first English bacteriologists to recommend the use of cotton-wool swabs for the isolation of diphtheria bacilli. By 1900 swabs were in common use (Kolle and Wassermann, 1903).

Although 50 years have now elapsed the bacteriologist can still give the clinician or the field investigator little information about the survival time of common pathogens on these simple appliances. It is generally agreed that the bacteriological examination should be done as soon as possible after swabbing; but this vague recommendation, however conservatively it might be interpreted, cannot always be met in practice. Van Reimsdijk (1924) studied the survival of diphtheria bacilli on swabs and found that by inserting the swab in a serum-agar gel contained in the holder tube the survival of these organisms was assured for 24 hours at room temperature. This method was cumbersome and has not been adopted. Brahdy *et al.* (1934) suggested dipping swabs in serum and incubating for four hours before culture and direct smear. Parish (1935) made a similar recommendation, but both these investigators were interested in developing a rapid method of diagnosis of diphtheria and not in extending the survival time of the organism on the swab.

Downie (1940) investigated various methods of prolonging survival of meningococci on nasopharyngeal swabs, and found that these organisms could be cultured 24 hours after swabbing, provided the swab was placed in contact with a blood-agar medium contained in the swab tube. Hynes (1942) stated that rectal swabs carrying intestinal pathogens should be cultured very soon after collection, or, if not, the swab should be kept moist by immersion in saline agar. Mitchell *et al.* (1946) described an elaborate method of prolonging survival of haemolytic streptococci, impossible for routine use, and Saint-Martin (1949) stated that gonococci would survive 4 to 18 hours on swabs if the latter were thrust into Hirschberg's medium immediately after swabbing. More recently, Aycock and Mueller (1950) recommended immersion of the swab in sterile horse blood for recovery of meningococci on delayed plating. Finally, none of the current textbooks in bacteriology or clinical pathology give any indication of the time limits for delayed culture of swabs.

It is evident from this survey of literature that this important problem requires further elucidation so that the results of delayed culture from swabs can be interpreted with some degree of certainty.

Laboratory Results

Two rather slight observations served as a starting-point of the present study. First it was noted that the survival time of *Str. pyogenes* on swabs from infected wounds was far greater than on throat swabs carrying the same organisms. The second observation was that 24-hour-old throat swabs mounted on wire were often discoloured by solution of the iron in the presence of saliva. The lines of investigation which followed soon showed that the former was a more fruitful approach to the problem of survival than the latter, which, however, could be easily overcome by discarding wire applicators for wood.

The experimental technique adopted involved inoculating a predetermined site on the swab with a tap-water suspension of the organism recovered from the centrifuged deposit of a 24-hour broth culture. The turbidity of the suspension was made equivalent to a thousand-fold dilution of No. 3 Burroughs Wellcome opacity tube. All swabs were mounted on wooden applicators and sterilized by autoclaving. Some were moistened before testing by immersion in sterile tap-water. Each swab was plated on an appropriate medium and then discarded, and the degree of growth was expressed according to the following key:

+ + + +	signifies	more than 200 colonies
+ + +	,,	50–200 colonies
+ +	,,	20–50 colonies
+	,,	5–20 colonies
±	,,	1–5 colonies
−	,,	no growth

The results of a typical experiment are recorded in Table I, which shows that two of the most important factors determining the survival of a given species were

TABLE I.—*Survival of Str. Pyogenes and Sh. Flexneri on Plain and Serum Swabs (Temperature of Storage, 17° C. to 22° C. Moistening Fluid, Sterile Tap-water)*

Organism	Type of Wool	Type and Condition of Swab	Degree of Growth on Plating at: 0 hr.	8 hr.	24 hr.	48 hr.
Str. pyogenes	No. 1 absorbent	Plain, dry	+ + + +	−	−	−
		,, moist		−	−	−
		Serum, dry		+ + +	+ + +	+ + +
		,, moist		+ + +	+ + +	+ + +
,,	No. 2 absorbent	Plain, dry	+ + + +	+ + +	+ + +	+ +
		,, moist		+	−	−
		Serum, dry		+ + +	+ + +	+ + +
		,, moist		+ + +	+ + +	+ + +
,,	No. 3 non-absorbent	Plain, dry	+ + + +	+ + +	+ + +	−
		,, moist		+ + +	−	−
		Serum, dry		+ + +	+ + +	+ + +
		,, moist		+ + +	+ + +	+ +
,,	No. 4 non-absorbent	Plain, dry	+ + + +	+ + +	+ + +	+ + +
		,, moist		+ + +	+ + +	+ +
		Serum, dry		+ + +	+ + +	+ + +
		,, moist		+ + +	+ + +	+ + +
Sh. flexneri	Nos. 1, 2, and 4	Plain, dry	+ + + +	−	−	−
		,, moist		+ +	+	−
		Serum, dry		+ +	+	−
		,, moist		+ + +	+ + +	+ +

the nature of the cotton-wool and the degree of moisture present. For example, it will be noted that the survival patterns of *Str. pyogenes* differed according to the wool used. With No. 1 sample of plain absorbent wool the organisms rapidly succumbed on both moist and dry swabs, whereas with No. 4 sample of plain non-absorbent wool viability was retained for at least two days. Samples 2 and 3 of absorbent and non-absorbent plain wools respectively were different again in that the presence of moisture accelerated death. In contrast, the survival of *Sh. flexneri* (Types 1, 2, 3, and 6 were tested) was unaffected by the different types of plain wool so long as the swab remained moist.

It was apparent in these and other experiments that the main characteristic of the survival of *Str. pyogenes* was its unpredictability on different samples of plain cotton-wool. However, the survival time of serum-treated swabs was constant and prolonged and uninfluenced by the nature of the wool or the presence of moisture. Although we have recorded growth in these experiments up to 48 hours, in many other experiments of a similar type it has been found that *Str. pyogenes* remained viable on serum swabs for at least 10 days. As a result of investigations of this type a serum-treated swab was developed which has been used as a routine in these laboratories for over four years.

Preparation of Serum Swabs.—Pledgets of cotton-wool (absorbent or non-absorbent) are rolled on wooden applicators (Peerless brand) and then dipped into ox serum for 10 to 30 seconds. The swabs are spread loosely on a sheet of blotting-paper and placed in a 37° C. incubator until dry (usually 30 minutes). The swab is then finished in the usual way by mounting in a 6 by ¼ in. (15 by 1.25 cm.) test-tube and sterilized by autoclaving for 20 minutes at 15 lb. pressure.

The finished product is a compact honey-coloured pledget, 3–5 mm. in diameter, in which the fibres are firmly bound to one another and to the applicator. It is therefore impossible to dislodge the wool when taking a specimen. The surface is smooth and does not unduly abrade the medium on plating. No special precautions are taken for storage purposes.

The above results (Table I), which have been repeatedly confirmed, foreshadowed the usefulness of serum swabs for a wider range of pathogenic organisms. In order to test this point plain and serum swabs were inoculated with suspensions diluted as indicated above and plated on appropriate media after 0, 8, 24, and 48 hours' storage at room temperature. Swabs plated immediately (0 hours) invariably produced a heavy growth—that is, more than 200 colonies. The results, listed in Table II, show the

TABLE II.—*Survival of Gram-positive and Gram-negative Organisms on Plain and Serum Swabs (Temperature of Storage, 16° C. to 22° C.; Moistening Fluid, Sterile Tap Water)*

Organism	Survival after Hours of Storage on: Plain Dry	Plain Moist	Serum Dry	Serum Moist
Gram-positive organisms:				
Str. pneumoniae, Type III ..	+ at 8	+ at 8	+ at 48	+ + at 24
Cl. welchii ..	+, 24	+, 8	+ +, 24	+ +, 24
C. diphtheriae gravis ..	+, 48	+, 8	+ + +, 48	+ + +, 48
Str. pyogenes ..	+, 48	+, 8	+ + +, 48	+ + +, 48
Str. viridans ..	+, 48	+ +, 24	+ + +, 48	+ + +, 48
Staph. aureus ..	+ +, 48	+ +, 24	+ + +, 48	+ + +, 48
Gram-negative organisms:				
N. meningitidis and *N. gonorrhoeae* ..	− at 8	− at 8	− at 8	− at 8
V. cholerae ..	−, 8	−, 8	−, 8	+, 24
H. pertussis ..	−, 8	−, 8	+ +, 24	+ +, 24
Sh. sonnei ..	−, 8	−, 8	+, 8	+ +, 48
Sh. flexneri and *Salm. typhi* ..	−, 8	+, 24	+, 24	+ +, 48
Pr. vulgaris ..	−, 8	+ + +, 24	+ + +, 24	+ + +, 48
Klebs. pneumoniae and *E. coli* ..	−, 8	+ + +, 48	+ +, 48	+ + +, 48

longest storage time up to 48 hours, at which a positive culture was obtained. They represent a summary of repeated experiments carried out at different room temperature and relative humidities.

The salient features brought out in this Table are: (1) With the exception of *Neisseria* serum swabs prolonged survival and yielded heavier growth (when compared with plain swabs) of all organisms tested (16 species). (2) Moisture tended to accelerate death rate of Gram-positive types on plain swabs but had no such effect with serum swabs. (3) In contrast, the survival of Gram-negative bacilli was favoured by moisture, and

PERCENTAGE MOISTURE CONTENT OF WOOL

this was even more pronounced on the serum swabs. (4) Of the Gram-positive cocci *Staph. aureus* survived best, then the streptococci, whilst the pneumococci tended to die off more rapidly. (5) Of the Gram-negative enteric bacilli *V. cholerae* was the most sensitive, while *Sh. sonnei, Sh. flexneri,* and *Salm. typhi* were intermediate in their survival times between *Vibrio* and the more resistant coliform types of the genus *Bacterium.*

Some interesting side-issues arose from these experiments which would appear to be worth recording. For example, the rapid death of Gram-negative enteric pathogens on plain dry swabs has not been sufficiently stressed in the literature or textbooks, and a clear-cut demonstration of this phenomenon is indicated. *Sh. flexneri* was used as being typical of this group of organisms, and serum and plain swabs were moistened with tap-water and examined, after storage at room temperature, under three sets of conditions. In the first series the moisture was retained by storing in sealed tubes; in the second, slow evaporation was allowed to proceed by plugging the swab tube, containing 1 to 2 ml. of water, with cotton-wool; and in the third rapid drying was achieved by exposing the swab direct to air. The rate of evaporation was determined by frequent weighing of eight swabs (four plain and four serum) in each series and viability determined by plating at 1, 2, 8, 24, and 48 hours. The results are shown graphically in the Chart. It will be seen that the death rate closely followed the rate of drying. For example, in curve 3 and in curve 1 (after unsealing) air-drying precipitated a sudden dying out of the organisms. While serum tended to lessen this lethal effect it must be emphasized that a high moisture content is the most important single factor in favouring survival of Gram-negative bacilli.

It is of interest to note that the behaviour of *Str. pyogenes* under the same conditions was quite different, in that rapid drying of the swab definitely favoured survival whilst slow drying associated with a high moisture content was unfavourable.

It is appropriate at this stage to refer to numerous survival measurements carried out with *Str. pyogenes* and *C. diphtheriae* using different moistening fluids. It was found that on certain batches of cotton-wool the rate of death was almost as rapid in the presence of saliva as with saline or tap-water and that this result could be effectively countered by serum treatment. Hence, from the clinical point of view, no reliance should be placed on the delayed culture—for example, 24 hours—of plain cotton-wool throat swabs, which are almost invariably moistened with salivary secretions (see Tables III and IV below).

Although it has been stated in several textbooks (e.g., Wadsworth, 1947; Mackie and McCartney, 1948) that absorbent wool should be used in preference to non-absorbent, our observations lend no support to this conclusion. In fact we are of the opinion that if a choice must be made the non-absorbent type of wool is preferable (see Table I).

In regard to the type of applicator, we have almost exclusively used the wooden applicator in preference to wire. The latter is unsuitable for serum swabs, as the serum discolours the wool in the presence of wire. With plain swabs no difference in survival time of *Str. pyogenes* was detected when wire and wooden applicators were compared, although Buchbinder *et al.* (1947) preferred the latter for sampling of food utensils.

In view of the work of Dunklin and Puck (1948) on the influence of relative humidity on the death rate of

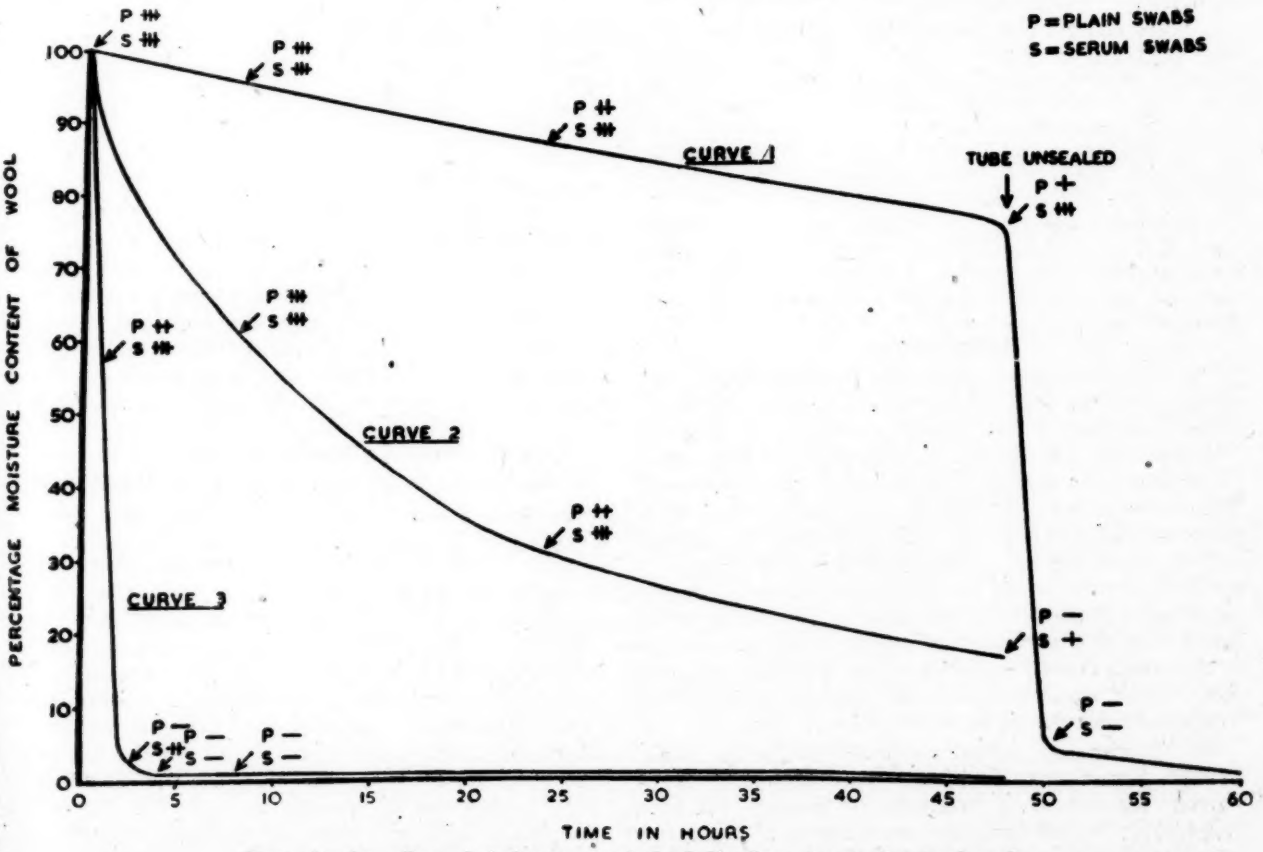

Chart showing effect of drying on survival of *Sh. flexneri* on cotton-wool swabs.

Gram-positive cocci in droplet spray, this factor was investigated in connexion with survival on swabs. Inoculated dry swabs were held between 18° C. and 23° C. in sealed containers over the solid and saturated solutions of various inorganic salts, anhydrous $CaCl_2$, and water to obtain the following levels of relative humidity: 0% R.H., $CaCl_2$ anhyd.; 35%, $CaCl_2.6H_2O$; 42%, $Zn(NO_3)_2.6H_2O$; 56%, $Ca(NO_3)_2.4H_2O$; 66%, $NaNo_2$; 90%, $ZnSO_4.7H_2O$; 100%, H_2O. Many tests were made using *Str. pyogenes* and *Sh. flexneri* as test organisms, but results were too variable to record in a tabular form. In general, it appeared that a high humidity (100%) favoured the survival of *Sh. flexneri*, and a low humidity (0%) favoured that of *Str. pyogenes*. Over the intermediate ranges the results were equivocal and we concluded that relative humidity, although it obviously plays a part in determining the rate of drying, was not a major factor in determining death or survival on plain swabs.

The influence of temperature variations was investigated over the ranges normally encountered in temperate climates—for example, 15° C. to 24° C.—and was found to be unimportant, except indirectly by affecting the rate of drying of moistened swabs. In spite of the fact that the preservation of *Shigella* requires the presence of moisture, refrigeration (4° C.) as a means of maintaining this is contraindicated. However, when survival of *Str. pyogenes* was compared at 4° C. and room temperature it was found, in contrast to *Sh. flexneri*, to be slightly prolonged at the lower temperature.

Other factors which have been studied may be briefly summarized as follows:

1. Anaerobiosis did not prolong survival. Hence it seems improbable that death on swabs is due to oxidation of cell constituents by atmospheric oxygen.

2. Ether and water extraction of absorbent and non-absorbent wools failed to alter survival when compared with untreated samples. Accordingly, serum protection does not operate by neutralization of toxic lipoid or water-soluble substances present in cotton-wool. This contention was further supported by noting that serum treatment improved the survival of *Str. pyogenes* on cellulose fibres other than cotton-wool—for example, filter-paper pledgets.

3. Colloids, other than serum, were tested, and it was found that treatment with egg albumen or ether-extracted serum was equally as effective as serum itself, but that 2% agar, 7% gelatin, 10% peptone, and 20% serum were ineffective.

Clinical Results

The foregoing experiments established the superiority of serum swabs over plain, and it now remained to apply these findings to clinical material. To this end a number of haemolytic streptococcal carriers were examined. The swabs were stored at room temperature in the dark for 24 and 48 hours, then plated on to gentian-violet horse-blood–agar medium and incubated for 48 hours. When serum swabs were included in a series these were always taken last. To obtain the results recorded in Table IV not more than four swabs were taken from any particular subject at a session, although two or three sets of swabbings were made on the same day. In all, approximately 650 swabs were examined. The results are shown in Tables III and IV.

To discriminate between plain and serum swabs (Table III) an analysis of the main factors (type of carrier, type of swab, and time of plating) has been considered. Combining the interactions of these factors, the experimental error was estimated. The results

TABLE III.—*Survival of Haemolytic Streptococci on Plain and Serum Throat Swabs (Temperature of Storage, 17° C. to 19° C.)*

Type of Streptococcal Carrier	No. of Subjects	Type of Swab	No. Positive After Storage for: 0 hr.	24 hr.	48 hr.
Light*	15	Plain	15	5	3
		Serum	15	15	9
Moderate† ..	16	Plain	16	10	5
		Serum	16	16	16
Heavy‡ ..	28	Plain	28	28	21
		Serum	28	28	27

* Fewer than 20 haemolytic streptococcal colonies on plating at zero time. † 20–50 colonies. ‡ Greater than 50 colonies.

indicated a significant superiority (at the 1% point) for serum swabs, particularly when swabs from light and moderate carriers are plated after 24 hours' storage.

During the course of this study an opportunity presented to investigate an outbreak of scarlet fever in a district 170 miles from Melbourne. Both plain and serum swabs from 44 individuals were examined 24 hours after swabbing, with the following results. With serum swabs Group A haemolytic streptococci were isolated from 39%, whereas only 23% of the plain swabs were positive. This incident illustrates the advantage to be gained by using serum swabs in the investigation of Group A haemolytic streptococcal infections.

Finally, we thought it necessary to show that our results for untreated wools were not due to a peculiarity of the wools available in Australia. In Table IV

TABLE IV.—*Survival of Haemolytic Streptococci on Swabs Prepared from Cotton-wools of Different Origin (Temperature of Storage, 17° C. to 19° C.)*

Origin of Wool	No. of Subjects	No. Positive After Storage for: 0 hr.	24 hr.	48 hr.
Edinburgh ..	18	18	10	5
Atlanta	18	18	7	4
Chicago	14	14	9	5
Liverpool ..	14	14	7	4
London	14	14	10	7
Melbourne ..	18	18	13	10
San Francisco ..	14	14	6	5

we record findings obtained by swabbing the same carriers with seven different wools procured in Australia, England, and the United States. Again the great variability of survival on plain wools is demonstrated, and the findings also show that the Melbourne brand of wool compared most favourably with any of the overseas types. The disappearance of oral flora was also assessed in this experiment, with results similar to those recorded for the haemolytic streptococci.

Discussion

It has already been pointed out that, apart from the well-known behaviour of meningococci and gonococci, a great deal of uncertainty exists concerning how long plating of swabs may be delayed before a significant change in the bacterial flora occurs. As a result of our experience we think it unwise to define any time limits when these refer to survival on plain cotton-wool swabs. This is subject to great variability even when standard inocula of pure cultures are used under controlled conditions. Apart from the number of cells on the original swab, these variations are largely due to the wool used and to the amount of moisture present. Neither of these factors can be adequately controlled in practice. To select a particular brand of cotton-wool, whether it be absorbent or non-absorbent, is no solution, as we

have found that different batches of the same brand of wool may yield significantly different survival patterns for most Gram-positive organisms. However, if we substitute serum swabs for the usual plain type then the first factor is automatically removed and the second becomes less critical. As a result, estimates of survival time on serum swabs may be accepted with greater confidence than those applying to untreated swabs.

Assuming a moderately heavy contamination of a serum swab (this is an important variable impossible to control clinically), we suggest that an examination may be expected to yield a valid result when cultured within the following time limits: (1) Organisms viable for less than eight hours: meningococci and gonococci. Downie's method or Aycock and Mueller's method is recommended for the former and Saint-Martin's for the latter. (2) Organisms viable for at least eight hours: *H. pertussis, V. cholerae* (moist swab is essential), *C. diphtheriae*. (3) Organisms viable for at least 24 hours: haemolytic streptococci, *Str. viridans, Cl. welchii*, pneumococci, *Shigella*, and *Salmonella* (moist swabs are essential for the last two genera). (4) Organisms viable for at least 48 hours: *Staph. aureus, Klebsiella, Proteus, Pseudomonas*, and *Escherichia* (moist swabs are essential for Gram-negative species).

The above estimates are based on laboratory experiments, but since the clinical findings for haemolytic streptococci closely paralleled the laboratory tests we consider that the same relationship will hold for most other organisms. However, in the case of *C. diphtheriae*, although good survival has been obtained in laboratory experiments (Table II), we do not recommend delaying plating longer than eight hours. In some clinical cases which we have examined the organisms failed to survive 24 hours on serum swabs.

Although autoclaved albumin-dipped swabs have not been studied so exhaustively the results were similar to those achieved with serum.

We have attempted to discover how serum prolongs survival, but without success. For instance, it could not be shown that serum inactivated a toxic lipoid or water-soluble agent in the wool or that it acted as a substrate for growth. The effect of serum protein is probably a physico-chemical one acting on the bacterial cells and prolonging their survival irrespective of the materials on which they are lodged.

It is felt that these findings may have a broader significance than the somewhat restricted object of this investigation. Two facts are worthy of consideration from an epidemiological point of view. The first is the rapidity with which enteric pathogens die off when dried in air, and the second is that organisms leaving their hosts in serous exudates will live longer than those discharged in secretions of low protein content. These two points may throw some light on factors determining the survival of pathogenic organisms outside their natural hosts.

Summary

A study has been made of the survival patterns of a large number of organisms on plain swabs under standard laboratory conditions. From this study the following conclusions have been drawn: (*a*) Survival time of Gram-positive organisms is variable, depending on the batch of cotton-wool used and the presence of moisture, the latter tending to accelerate rate of death. (*b*) Survival time of Gram-negative enteric pathogens is uninfluenced by the type of wool but depends on the degree of moisture on the swab. On moist swabs survival is greatly prolonged.

A new type of swab was developed, termed a serum swab, on which survival times of all organisms tested, except the *Neisseria*, were increased.

Other factors such as temperature of storage, relative humidity, and anaerobiosis were investigated and found to be relatively unimportant.

The mechanism of serum protection is unknown.

We wish to record our thanks to Margaret Gibson, M.Sc., for her assistance in the early stages of this work and to the various laboratories who sent us specimens of their cotton-wools.

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INVESTIGATION INTO THE EFFECTS OF AUREOMYCIN AND CHLORAMPHENICOL IN HERPES ZOSTER

BY

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Recent advances in antibiotic therapy have been sufficiently great to produce an effective remedy against most bacterial infections, and it is therefore natural that the effects of antibiotics on virus infections should be put to the test. Particular success accompanied such an investigation in the case of "aureomycin" and virus pneumonia. Finland *et al.* (1949) have described the effects of aureomycin on the course of 24 cases of herpes zoster; they conclude that this drug increases the rate of healing of the skin lesions, causes a rapid subsidence of herpetic pain, and seems to be followed only rarely by post-herpetic neuralgia. No controls were used in their series, and the total dosage for each case varied from 7.4 to 54 g. From this evidence they conclude that an effective dose might be 4 g. daily for two to four days followed by 2 g. daily for a further three to five days, and that particular benefit results if the treatment is begun early. They claim that in most of the patients there was no evidence of secondary infection, that no new lesions developed after the first day or so of treatment, and that pain was relieved after the first day.

Dawson and Simon (1949) have reported beneficial effects from the use of chloramphenicol in a small controlled series of cases, and Binder and Stubbs (1949) administered aureomycin to four cases of zoster and obtained satisfactory results in three and a fair result in the fourth. One patient, a child of 11, developed poliomyelitis five days after the subsidence of the zoster rash. Their dosage scheme was only 2 g. daily for two days for the adults and half this for the child.

Case (1949) has described good results in one patient, and Brainerd *et al.* (1949) were impressed by the rapid improvement of a case of herpes ophthalmicus similarly treated. In view of these claims and in spite of the difficulties of assessing the effects of treatment on a syndrome of such varying severity as herpes zoster, the following small controlled investigation was carried out.

Material and Method

The material comprised every case of herpes zoster admitted to Ashford Hospital, Middlesex, between June, 1950, and March, 1951. The local doctors were asked to send in all cases except those whose rash had been present for 14 days or more. Mild cases either refused to come in or had been unrecognized. The patients were nursed in the acute medical wards, and no case of zoster or varicella occurred in other patients, although doctors were asked to watch for possible contact cases in the district. This request produced the interesting observation that in 8 out of the total 44 cases chicken-pox occurred in one or more of the patients' children from 8 to 14 days after the patient's admission to hospital.

The investigation was divided into two parts. First, a series of 11 controls (group 1) treated with a placebo (glucose) made up in capsules to resemble aureomycin was compared with a series of 11 cases (group 2) treated with aureomycin 2 g. daily for six days. Secondly, a similar series (group 3) treated with a larger dose of aureomycin for a shorter period (4 g. daily for four days) was compared with a series (group 4) treated with chloramphenicol 2 g. daily for six days.

There were therefore four groups of 11 cases each. Group selection for each case was made at random by the sealed-envelope method suggested by Professor Bradford Hill, so that only the hospital dispenser knew which cases were the controls. Daily records were kept on a standardized form regarding pain, paraesthesiae, sleep, extent and severity of rash, including amount of secondary infection and any side-effects noticed by the patients. Cases were divided into two grades, "severe" and "moderate," based on the severity of pain and extent of the rash; and, because of the variations in the description of subjective symptoms, only the simplest terms were used. Local treatment was confined to talc powder to prevent sticking, and only three analgesic drugs were used—codeine, pethidine, and "omnopon."

Because of the cost and the possible side-effects, just enough antibiotic was given to control the infection, and the dosage was standardized for purposes of comparison of effect and for simplicity of administration. Long *et al.* (1950) consider that dosage schedules are well established, and suggest that for moderately ill patients the total daily maintenance dose of aureomycin should be from 20 to 30 mg. per kg. body weight. They suggest that the drug is best given at six-hourly intervals and that there is no need for a loading dose. The length of treatment has not been defined, and an arbitrary figure of six days was used in the present series.

In the first treated group, 0.5 g. of aureomycin at six-hourly intervals was given to each patient for six days—a total of 12 g.—so that a patient weighing, say, 147 lb. (66.7 kg.) would be receiving 30 mg. per kg. as a daily maintenance dose; in the second treated group twice this dose was given for four days, so that these patients were receiving 4 g. daily and 16 g. in all. At first 1 g. was given six-hourly; but this dosage produced severe side-effects, and so 0.5 g. was given three-hourly, the dose being doubled late at night to save waking the patient. In the chloramphenicol group the dosage was the same as in the first aureomycin group.

Table I shows the comparability of the groups in some other respects; although the numbers are small the similarity is great.

TABLE I.—*Showing Comparability of Groups Before Treatment*

Group	No.	Sex		Average Age of Patients	Average Age of Rash on Admission	Severity		Location	
		M	F			Severe	Mod.	Spinal	Ophth.
1	11	7	4	56 yrs.	4·6 days	6	5	7	4
2	11	5	6	54 ,,	4·3 ,,	6	5	8	3
3	11	8	3	50 ,,	4·1 ,,	5	6	7	4
4	11	7	4	51 ,,	4·4 ,,	4	7	7	4

Course of Untreated Cases

Before the results are analysed the natural history of herpes zoster, shown by the course of the illness in the untreated cases (group 1) and by the history and condition of all the groups before treatment, is worthy of attention.

Prodromal symptoms of malaise and fever were uncommon, and generalized headache occurred in only one of the spinal cases. The first symptom was in many cases irritation with occasional sharp stabs of burning pain, usually in the place where the rash afterwards appeared. The average time between this first symptom and the onset of the rash in all groups was 4.5 days, although in 7 of the 44 cases the rash accompanied the first twinge of pain. The longest interval between pain and rash was 12 days. In three cases the initial pain was located some few segments higher than the subsequent rash, though always on the same side.

In the 15 ophthalmic cases generalized headache was common and at times was accompanied by nausea and vomiting; it was followed by neuralgic pain and irritation over the distribution of the ophthalmic nerve.

The rash itself began as a patchy erythema with oedema of the skin, and, after a short papular stage which was sometimes absent, vesiculation occurred in clusters, usually in the middle of a patch of erythema. When close to each other the vesicles tended readily to coalesce, and if of any size became rapidly haemorrhagic. Fresh vesicles appeared in some cases up to the fifth day of the rash, and these were often seen alongside haemorrhagic and pustular lesions.

On the third or fourth day pustulation occurred, apparently due to a varying degree of secondary infection with staphylococci, and these pustules either ruptured, leaving in some cases a blackish almost gangrenous appearance of encrustation, or began to dry up. This crusting usually began on the fifth to the eighth day of the rash, was complete within thirteen days except in two severely infected cases, and was followed by desquamation, separation of the crust, and eventual fading of the rash.

Pain was, of course, a prominent feature, varying from aching and soreness to pain of great severity variously described as burning, gnawing, drawing, shooting, jumping, or neuralgic. The pain was worse at night, was aggravated by movement or light touching of the skin, was paroxysmal, and could often be relieved by heavy pressure on the skin. It was at its height while vesiculation was occurring and lasted throughout the pustular stage, beginning to fade when crusting started, and leaving an ache or soreness when the crusts had fallen off.

Paraesthesiae were always present, and were variously described as irritation, itching, burning, tenderness, tingling, prickling, feelings of stiffness, bruising and heaviness, occasional pins-and-needles, a feeling of rawness, numbness, and thumping. They often persisted longer than the pain and seemed to match in intensity the severity of the rash. In the ophthalmic cases pulling or combing the hair caused "electric shocks" to be felt in the head; these were very distressing.

Objective neurological changes were increased sensitivity to light touch and pinprick in the erythematous and vesicular stage, with decreased sensitivity often amounting to complete loss of feeling in the scars after desquamation.

The cerebrospinal fluid was examined before treatment in every case; if abnormal, examination was repeated, usually at weekly intervals. Of the 44 cases, 14 had abnormal C.S.F.—10 of these were ophthalmic cases, and the other four were very severe spinal cases in which the rash extended over two or three segments.

TABLE II.—*Details of Abnormal Cerebrospinal Fluids*

Age	Case No.	Group	Type	Days after First Rash	Cerebrospinal Fluid			
					Protein mg./100 ml.	Cells per c.mm.		
						Total	Polys.	Lymphs.
76	16	2	Spinal	8	75	34	18	16
				15	20	27	—	27
				22	20	18	—	18
79	25	2	Ophthal.	7	70	40	24	16
				16	20	2	—	2
70	34	2	,,	9	210	45	20	25
				16	50	40	16	24
				24	25	42	—	42
69	29	1	,,	4	50	16	10	6
				11	20	12	4	8
				18	20	5	—	5
59	23	1	,,	5	110	24	16	8
				12	50	36	12	24
				20	30	12	—	12
63	26	1	,,	6	90	36	20	16
				13	40	28	8	20
				21	20	12	—	12
70	29	3	,,	5	90	44	24	20
				12	40	30	12	18
				19	20	10	—	
64	30	3	,,	4	80	62	40	22
				11	20	20	8	12
				18	20	8	—	8
58	19	2	Spinal	10	70	26	6	20
				18	30	10	—	10
54	31	3	Ophthal.	4	70	25	15	10
				11	20	12	—	12
				18	20	4	—	4
53	7	3	Spinal	4	50	45	30	15
				11	40	20	8	12
				15	20	10	—	10
70	41	4	Ophthal.	6	75	36	14	22
				13	30	30	—	30
				20	20	8	—	8
63	22	4	Spinal	4	90	44	20	24
				11	40	20	—	20
				18	22	2	—	2
60	38	4	Ophthal.	5	75	28	10	18
				12	40	6	—	6
				19	20	6	—	6

Of the 30 with normal C.S.F., 25 were spinal cases and 5 were mild ophthalmic cases. Thus of the 29 spinal cases in this investigation only 4 had abnormal C.S.F., and of the 15 ophthalmic cases 5 had normal C.S.F. The abnormal fluids are detailed in Table II, in which the high protein in the early stage of illness is to be noted. The average age of the patients with abnormal C.S.F. was 64, whereas that of the whole series was 53.

Analysis of Results

In the first 22 cases an attempt was made to guess whether the patient was having placebo or aureomycin, and the condition of the rash was used as a guide—13 guesses were correct, 2 were incorrect, and in 7 no reasonable guess could be made.

One particular case merits detailed description. A man aged 65 was admitted seven days after he had noticed a neuralgic pain in his right forehead which kept nagging at him particularly at night and made him keep rubbing his forehead. Two days before admission he noticed a red rash on his forehead and his right eyelid began to swell. On admission the whole of the right forehead was swollen and red; chemosis of the lids and conjunctival injection were present, but the cornea was clear. There were two moderate-sized vesicles and one papule on the forehead, and he complained of fairly severe burning and neuralgic pain on the right side of the head. Light touch made the pain worse and heavy pressure relieved it. The right corneal reflex was slightly reduced.

The next day there were five haemorrhagic vesicles, the pain was less, and he noticed "electric shocks" when his hair was combed on the right side. On the third day of treatment there were three more clusters of small vesicles, the pain was moderate, and the paraesthesiae were less marked. Sleep was normal without sedatives, and he was cheerful and ate well. The chemosis of the lid began to go, no further lesions appeared, and the pain changed to a bruised feeling which disappeared on the sixth day of treatment, when drying and crusting of the rash began, being complete on the ninth day. On the thirteenth day separation of the crusts was complete, and he went home feeling well except for a slight sensation of bruising over the right outer canthus. His C.S.F. contained 10 lymphocytes per c.mm. and 60 mg. of protein per 100 ml.

This case is described in detail because it was thought probable that an attack of ophthalmic zoster had been "aborted" by aureomycin about the fourth or fifth day. Actually he had been receiving the placebo. This sort of case should be borne in mind when remedies are alleged to "cut short" or "abort" an attack of zoster.

Comparison of Rash

Fresh vesicles appeared in all of the controls that were admitted within 72 hours of the onset of the rash. These continued to appear up to the fifth day of observation. In four similar cases of group 2 admitted within 72 hours, fresh vesicles appeared up to the fourth day of observation. One of these cases received aureomycin within 48 hours of the appearance of the rash, and in spite of this fresh lesions occurred. In the cases receiving a higher dosage of aureomycin (group 3) four showed a few fresh lesions up to the third day of observation. These four cases were admitted on the third (two cases), fourth, and fifth days of their rash. Fresh vesicles were seen in two of the chloramphenicol cases up to the fourth day of the rash.

These figures suggest that treatment had a slight but not significant effect on the early cutaneous manifestations. It was hoped that bacteriological control would be possible, and that it could be shown whether the

virus could be grown from the vesicles of the treated cases as it can from the untreated; but Professor Bedson through the Medical Research Council and Dr. Weston Hurst in a personal communication have stated that this procedure is impracticable.

The average time taken for the rash to become crusted and completely dry was 13 days in group 1 (controls), 11 days in group 2, and 10 days in group 3 and group 4. The difference in the first two groups was due mainly to four cases in which aureomycin had been given within three days of the rash appearing: in these the rash was dry in eight days. One case in group 3 is excluded, as it showed no vesiculation at all and progressed most dramatically from papules and erythema to recovery.

The most marked difference between the controls and the treated cases was seen in the occurrence and control of secondary infection. This infection was universal in the controls, and often it was very severe. Staphylococci were grown from the vesicle fluid in all the controls, but not in the treated cases while they were receiving aureomycin or chloramphenicol. One very severe case was of interest in this connexion.

A woman aged 76 was admitted with a very severe zoster of some eight days' duration affecting D12 and L1 on the left side. She was very ill, and the case was complicated by hypertension and diabetes mellitus. The rash was heavily infected with staphylococci. She received aureomycin, 2 g., daily for six days. On the fourth day of treatment vesicular and pustular fluid was sterile. Two days after treatment had been discontinued the rash looked grossly infected again and the fluid once more grew staphylococci in profusion.

Early treatment seemed to prevent any secondary infection and shortened the time from the first sign of the rash to complete desquamation. In the control group this averaged 24 days and in the treated groups 20 days. In those cases (10) treated within 72 hours of the rash appearing, desquamation was complete in an average of 15 days.

Pain

Comparison of a symptom that is wholly subjective is always beset with difficulties. The duration was measured simply by asking whether pain—not paraesthesiae—was present or not, and a note was made of the first pain-free day and the first good night's sleep unaided by drugs. The severity was roughly gauged by the need for analgesics; the drugs allowed were limited to three, and a standard dose used in each case—

TABLE III

Group	First Pain-free Day	First Unaided Normal Night's Sleep	No. of Patients Receiving			
			Omnopon	Pethidine	Codeine	Nil
1	12th	9th	3	6	7	2
2	11th	10th	3	5	8	2
3	12th	6th	1	2	9	2
4	11th	7th	2	3	7	2

omnopon 1/3 gr. (22 mg.), pethidine 100 mg., and tab. codein. co. (two tablets). An analysis is given in Table III. It shows that there was no significant difference between groups 1 and 2, but groups 3 and 4 required less analgesic and slept better.

Paraesthesiae

Perhaps of all the symptoms of herpes zoster the severity and duration of the paraesthesiae give the truest picture of the effects of viral infection on the nervous system. These paraesthesiae are usually clear-cut, easy to define by the patient, and independent of pain sensitivity, which is always one of the factors which make the assessment of pain so difficult. They were of two kinds—those spontaneously experienced by the patient without stimulus, and those in which stimuli affecting the skin and deeper structures were wrongly interpreted. The former type lasted longer than the latter and occurred more often in the ophthalmic than in the spinal cases.

Comparison of the groups showed no difference between the treated and the untreated cases in the whole series, nor was there any significant lessening of severity or duration in the four cases in group 2 treated within 48 hours of the appearance of the rash.

This result suggests either that this treatment has no control over the virus in its effects on the nervous system or that the damage has already been done when the skin manifestations appear.

Side-effects

The side-effects of these antibiotics have been described by Harris (1950) and Tomaszewski (1951) among others, although in most of their cases the dosage was greater and was spread over a longer period than in this series. Probably because of this the side-effects have been less noticeable in our cases.

Toxic Effects

Nausea and vomiting occurred with approximately equal frequency in the controls, chloramphenicol cases, and lower-dosage aureomycin cases. In the higher-dosage cases, nausea and vomiting were very troublesome at first with 1 g. six-hourly, but became less severe when 0.5 g. was given three-hourly.

Loose stools occurred in four aureomycin and two chloramphenicol cases within the first two days of treatment but did not persist beyond the fourth day. True diarrhoea did not occur; no granulocytopenia was encountered, although white-cell counts were done on all patients; and depression was no more than could be expected from the underlying illness. Hypersensitive reactions did not develop in any case, and no rash occurred that could be attributed to the drug.

Effects Due to Bacterial Sterilization

Aureomycin and chloramphenicol effectively sterilize the alimentary tract from mouth to anus, and it is suggested that some of the effects mentioned below may be due to the unrestricted growth of fungus in the absence of bacterial competition, rather than to vitamin-B deficiency as has been suggested. It is of course essential to support antibiotic therapy of long duration with vitamin-B complex owing to interference with the normal synthesis of this vitamin if the upper intestine is sterilized, but it seems unlikely that there would be clinical evidence of avitaminosis within a few days. Similar effects have been described in penicillin treatment (Geiger *et al.*, 1946), and evidence of fungus infection was obtained in those cases in the present series which showed this type of side-effect.

In four cases (three women, one man) redness of the oral mucous membrane and tongue appeared on the third and fourth days, and the patients complained of a metallic taste. Two were treated with aureomycin and two with chloramphenicol.

One man and one woman had black tongues after 8 g. and 10 g. of chloramphenicol respectively: in the former

the condition was more severe, with well-marked hairiness of the tongue, and in both patients the dark-brown pigmentation could be seen spreading forward like two fingers over the surface of the tongue on both sides of the median fissure. Tongue scrapings showed a dark monilia in the man and *Candida albicans* in the woman, with no bacterial flora. Angular fissuring of the mouth with buccal ulceration occurred in one case, and anal irritation and soreness in three cases, including the two with black tongues, and one in which anal scrapings showed the presence of *Candida albicans*.

Discussion

The general results of this controlled series show little difference between treated and untreated cases with regard to the appearance of fresh herpetic lesions, the amount and duration of herpetic pain, or the type, duration, and frequency of paraesthesiae.

Further analysis shows that treatment with either aureomycin or chloramphenicol within the first week of the rash modifies the duration of the pustular stage and is associated with earlier drying and earlier desquamation. This effect can reasonably be attributed to the action of these antibiotics on the secondary infection, particularly if it is very severe. This action was remarkably consistent, as, in all cases in the aureomycin groups and all but two of the chloramphenicol group, cultivation of the vesicle or pustular fluid was sterile. In the two chloramphenicol exceptions, only a scanty growth of *Staphylococcus albus* was obtained.

In view of these results it seems unjustifiable to use such expensive drugs in the routine treatment of herpes zoster. It is suggested that their use be confined to two types of patient—one the severe case of ophthalmic zoster, particularly in the elderly, where it is possible that secondary infection plays some part in the severity of the scarring and even of the post-herpetic pain which so commonly follows; the other the severe case of spinal zoster involving two or more segments, where the patient's life may be endangered by the toxic effects of severe secondary cutaneous infection. Diabetic and nephritic patients particularly come into this category.

There is less evidence to support the use of these drugs in the very early stages of this illness, before the rash is established, in the hope that the virus may not yet be completely fixed and may therefore be more vulnerable. A much larger series would be required before enough of these early cases could be found for statistical investigation, and, although no such evidence has appeared here, the following case merits description:

A man aged 54 (Case 31) was admitted on November 3, 1950, with a history of five days' pain behind the right ear and extending to the forehead; it was paroxysmal in character and was relieved by rubbing. This was followed by irritation, redness, and swelling of the right side of the forehead two days before admission. On examination there was a red swollen area over the right forehead extending a little way over the midline with one or two papular collections and three pinpoint vesicles. The right eye was normal and the corneal reflex unimpaired. Aureomycin, 0.5 g. three-hourly for four days, was begun. He described his pain as moderate and said that his forehead felt tender and heavy. He was given pethidine and codeine the first night. The next day his condition was unchanged and he slept well unaided. The third day the swelling was gone and the erythema fading. The fourth day he had no pain, no tenderness, only a moderate feeling of heaviness, and the edges of the rash were no longer recognizable. On the fifth day the three pinpoint vesicles were crusted, and by the seventh day the rash and paraesthesiae had disappeared, leaving only a slight hypoaesthesia where the rash had been. There was naturally some question whether this was a case of ophthalmic zoster, but the cerebrospinal fluid was typical, as can be seen from Table II.

Summary

Forty-four consecutive patients suffering from herpes zoster have been investigated to determine the effects of aureomycin and chloramphenicol on the course of this condition.

These patients were divided into four groups of 11 each: group 1, the controls, receiving glucose; group 2, aureomycin orally 2 g. daily for six days; group 3, aureomycin 4 g. daily for four days; and group 4, chloramphenicol 2 g. daily for six days. The controls were selected at random and the observers did not know which patients were in this group.

The results showed that there was no significant difference between the groups in respect of pain, paraesthesiae, or the appearance of fresh herpetic lesions. The treated groups were free from secondary infection, which was present in every one of the controls, and this freedom may have modified the pustular stage of the rash so that desquamation was earlier and scarring less.

Two cases in which treatment seemed to bring about a dramatic amelioration of symptoms are described in detail: one was a treated case and the other a control.

It is suggested that in view of these results there is no justification for the routine use of such expensive drugs in herpes zoster, and that they should be employed only in very severe cases, particularly ophthalmic zoster, occurring in elderly or debilitated patients.

I should like to thank my colleagues on my medical firm for their help in observing and treating these patients; Professor Bradford Hill and Dr. J. Knowelden for suggesting the sampling method of selection of controls; the Antibiotics (Non-Tuberculous) Trials Committee of the Medical Research Council for supplies of aureomycin; and the general practitioners of this area for sending me the patients.

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Special ceremonies at the University of Copenhagen on April 27 marked the successful conclusion of the first course at the W.H.O. International Training Centre for Anaesthesiology. The Centre, founded just a year ago, is the first major training project established by the World Health Organization to aid medical science in Europe. Thirty medical Fellows from seven European nations made up the graduating class. They are all doctors or surgeons who are now returning to their own countries to teach the new techniques of modern anaesthesiology. A second group of 30 Fellows, like the first group supported for the most part by W.H.O. fellowships, arrived in Copenhagen on May 3 for the next year's course.

EXPECTANT TREATMENT OF PERFORATED PEPTIC ULCER*

BY

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The surgical treatment of acute perforated peptic ulcer has through the past three decades gradually tended to become more conservative. Even the method now generally employed at most surgical centres in this country—simple closure of the perforation by suture or an omental plug without any attempt at careful peritoneal toilet or drainage—has often seemed an almost unnecessary procedure. Surgical intervention sometimes seems to do more harm than good. When operating on such patients every surgeon of experience must often have noticed that the perforation had already undergone spontaneous closure. In most instances this seems to be due to adhesions between the bowel and the under surface of the liver, though occasionally the hole is found to have been sealed successfully by omental adhesions alone. In these circumstances one has often had the feeling that to separate the adhesions and then to suture the perforation is defeating the ends which have already been achieved by the natural healing processes of the body.

The articles of Tayor (1946) and Visick (1946) therefore excited my interest. But it appeared to me that most previous attempts to secure a control series of such cases treated conservatively had been vitiated by limiting the selection to particular clinical varieties. If this method of treatment was to be of use in modern surgery, it seemed that its potentialities ought to be fully investigated by employing it on a sufficiently large unselected series of cases. Moreover, the suggestion in Taylor's article, that conservative measures should be reserved for patients whose stomachs are relatively empty at the time of perforation, did not seem logical. The degree of peritoneal soiling ought to make no difference to the success or failure of conservative measures, provided that any remaining stomach contents are aspirated before expectant treatment begins, as it is never possible to remove all the food debris from the peritoneum even at laparotomy. Nor should the length of time between onset and admission to hospital have any influence on the success of such treatment.

Most of the experimental work on the bacteriological content of the stomach during an acute exacerbation of peptic ulcer suggests that infection is invariably present, so that the accepted division of the resultant peritonitis into an early aseptic and later septic stage would appear to be incorrect. In any case, experience of penetrating war injuries of the abdomen complicated by gross peritoneal soiling and of the surgery of acute abdominal inflammatory conditions shows that the peritoneum is able to deal with an amazing degree of septic contamination provided that this does not continue to take place. It was undoubtedly the progressive irritation of the peritoneum by infected gastric contents which was mainly responsible, before the days of chemotherapy, for the high post-operative mortality in cases of perforation in which there had been a long time delay between onset and operation.

*A paper read at the inaugural meeting of the West Midland Surgical Society at Leicester on January 13, 1951.

It seemed, therefore, that there would be little additional risk to the patient if expectant measures were employed on every occasion, provided that the stomach was kept empty and that laparotomy was immediately instituted if the clinical condition failed to respond satisfactorily to this treatment. Encouragement to follow this course was given by two further clinical observations. It has been no infrequent experience to note, during routine operative procedures for peptic ulcer, the presence of adhesions suggesting spontaneous sealing of an undiagnosed acute perforation. Further, simple conservative measures have proved surprisingly successful in a number of cases of acute perforation in which the patient's general condition or some concomitant disease contraindicated operative treatment.

Between October, 1947, and October, 1950, therefore, all cases of acute perforated peptic ulcer admitted to my wards were primarily treated conservatively, no attempt being made to select them from the point of view either of time interval between onset and admission or of the length of time after a meal when the perforation occurred. In order, however, to ensure that only true cases of perforation should be included, patients who failed to satisfy the following criteria have been discarded from this series: (1) Those who did not give a classical clinical picture of perforation; (2) those who failed to show the typical picture of gas under the diaphragm on *x*-ray examination after the institution of

TABLE I.—*List of Cases*

Case	Age	Sex	Time Interval between Onset and Admission (Hrs.)	Time to Settle (Hrs.)	Chest Complications	Type of Ulcer	Remarks
1	38	M	12	20	No	Duodenal	
2	57	M	6	(48)	Yes	Anterior gastric	Laparotomy. Death 48 hours later
3	35	M	6	36	,,	Duodenal	
4	57	M	24	24	,,	,,	
5	43	M	18	30	No	High lesser curve gastric	
6	42	M	3	22	Yes	Duodenal	
7	68	M	26	36	No	,,	
8	37	M	7	24	,,	,,	
9	52	M	9	32	,,	,,	
10	61	M	5	(12)	,,	Anterior duodenal	Death during expectant treatment
11	36	M	3	(24)	,,	Anterior gastric	Laparotomy. Recovery
12	26	M	3	36	Yes	Duodenal	
13	46	M	5	18	,,	,,	
14	43	M	7	22	No	,,	
15	32	M	2	28	Yes	,,	
16	38	M	4	42	,,	,,	
17	65	M	22	30	No	,,	
18	48	M	3	16	Yes	,,	
19	43	M	5	44	No	,,	
20	33	M	4	24	,,	,,	
21	45	M	9	14	Yes	,,	
22	21	M	3	20	No	,,	
23	21	M	2	14	Yes	,,	
24	68	M	5	32	No	,,	
25	55	M	3	28	Yes	,,	
26	37	M	9	31	No	,,	
27	37	M	8	17	,,	,,	
28	52	M	4	48	Yes	Carcinoma stomach	Inoperable at *x*-ray later
29	30	M	5	18	No	Duodenal	
30	46	M	5	(48)	,,	Anterior gastric	Death during expectant treatment
31	29	M	3	14	,,	Duodenal	
32	24	M	4	34	,,	,,	
33	47	M	3	25	Yes	,,	
34	36	F	18	34	No	,,	
35	72	F	2	(24)	Yes	Anterior gastric	Laparotomy. Death 72 hours later
36	28	M	21	18	No	Duodenal	
37	45	F	4	34	,,	,,	
38	47	M	7	19	,,	Low lesser curve gastric	
39	44	M	6	22	,,	,,	
40	38	M	3	13	,,	Duodenal	

Figures in parentheses denote time when laparotomy was done or when death occurred.

treatment; and (3) those on whom subsequent barium-meal examination of the stomach and duodenum failed to show either the scar of a healed ulcer or continuing ulceration. It was felt that only in this way could indefinite clinical conditions such as "acute exacerbation of peptic ulcer" and "subacute leaking perforation," which do not represent accurate clinical entities, be satisfactorily excluded. In all, 40 cases (37 male, 3 female) have satisfied these provisions. Table I gives details of all cases. Table II shows the age distribution and also the time interval before beginning treatment.

TABLE II.—*Age Distribution and Time Interval Between Onset and Admission*

Age	No.	Time Interval	No.
20–29	6	Under 5 hours	17
30–39	12	5–9 ,,	16
40–49	12	10–14 ,,	1
50–59	5	15–19 ,,	2
60–69	4	20–24 ,,	3
70 and over	1	25–29 ,,	1

The youngest was aged 21 and the oldest 72.

Treatment

The treatment employed on all these patients was immediate aspiration of any remaining stomach contents on arrival at hospital, followed by continuous Wangensteen gastric suction by means of an intranasal Ryle's tube of modified design, with additional perforations over its lower 10 in. (25 cm.). Intramuscular injections of morphine, 1/6 gr. (11 mg), were given six-hourly and intravenous infusion was instituted. Continuous gastric suction is essential in order that the stomach and duodenum may be kept as empty as possible of secretion and regurgitated intestinal content until effective sealing of the perforation has had every chance to take place, and to counteract any gastric dilatation which might result from air-swallowing. Provided that one has staff who understand the method, it is also much easier from the nursing angle than the less effective procedure of intermittent aspiration. The amount of fluid given intravenously was 3 litres in every 24 hours—a continuous rotation of 5% glucose-saline, plasma, and normal saline. In addition, all cases were treated with injections of penicillin, 500,000 units being given in divided doses each 24 hours.

This treatment was continued until the acute symptoms settled. After a varying time the board-like rigidity of the abdomen disappeared and the muscles gradually relaxed. This took place first on the left side of the abdomen and later in the epigastric region and right iliac fossa. Some residual tenderness and guarding always remained in the epigastrium and down the right flank to the right iliac fossa for several days, gradually passing off as the peritoneal inflammation resolved. The associated clinical evidences of recovery were a falling pulse rate and the advent of active bowel sounds on abdominal auscultation. Table III shows the varying periods of time required for the acute symptoms to settle. It will be noticed that, out of the 35 successful results of expectant treatment, 27 cases settled within the first 30 hours and only 3 had failed to respond by the end of 36 hours.

TABLE III.—*Time Taken to Settle Under Expectant Treatment (Excluding Cases Dying or Operated on)*

	No.		No
12–18 hours	9	31–36 hours	5
19–24 ,,	9	Over 36 ,,	3
25–30 ,,	9		35

The shortest time was 13 hours and the longest time 48 hours.

After the improvement in the patient's clinical condition showed that no further leakage was taking place from the perforation, inferring that adequate closure had occurred, he was placed on an early Meulengracht diet, which was rapidly increased to full gastric diet within a week. Ambulation was not allowed until all tenderness in the right iliac fossa had disappeared, which usually took about a week, but progress after this stage was always rapid and the average length of time in hospital was only 10–12 days. It was not considered safe to carry out the subsequent barium-meal examination for at least a further month, so that the patients were discharged home on continued medical regime for this period and attended the out-patient department later for their gastro-intestinal *x*-ray examination. I have personally witnessed an instance of the secondary perforation of a duodenal ulcer under the *x*-ray screen as the result of an improvidently early barium-meal examination.

Indications for Operative Intervention

This paper has deliberately been entitled "Expectant treatment of perforated peptic ulcer" because I believe that there is no place in surgery for purely conservative treatment, except possibly in very late cases whose poor general condition precludes any attempt at operation. All cases should invariably be carefully watched and kept constantly under review during the first 48 hours of expectant treatment, with a view to operative intervention should they fail to show obvious clinical improvement. The indications for laparotomy are failure of the abdominal rigidity and tenderness to pass off, and a pulse rate which either does not fall satisfactorily or continues to rise.

Accurate assessment of the clinical condition of these cases is not as difficult as might be imagined and does not seem to be unduly influenced by the morphine administered. Even the ward nursing staff were soon able to decide with considerable accuracy whether a patient was responding effectively to treatment. Actually, most cases which were going to settle satisfactorily showed obvious indications of doing so within the first 12 hours, even if their subsequent improvement was tardy or intermittent.

Results

Table IV gives an analysis of the results. Operative intervention was indicated only as a secondary procedure in three cases.

TABLE IV.—*Analysis of Results*

	Total No. of Cases	No. Recovered
Duodenal ulcer	32	31
Gastric ulcer:		
Lesser curve	3	3
Anterior	4	1
Gastric carcinoma	1	1
Total	40	36

Case 2.—A man aged 57 had a six-hour history of perforation before admission. He appeared to settle satisfactorily during the first 12 hours of expectant treatment but failed to maintain this improvement, so that laparotomy was carried out at the end of 48 hours. He was found to have a large anterior gastric perforation, which appeared

at first sight to have localized by adhesions between the stomach and the anterior abdominal wall. This localization, however, proved not to be complete, and the resultant local collection of fluid was leaking slowly into the general peritoneal cavity. On separation of the adhesions a perforation measuring nearly 3 in. (7.5 cm.) in diameter was found, and was closed only with considerable difficulty. Death occurred within the next 48 hours from cardio-renal failure, probably secondary to toxaemia from his peritonitis.

Case 11.—A man aged 36 had a three-hour history prior to admission. He failed to improve enough by the end of 24 hours to justify continued expectant treatment. Laparotomy was therefore carried out, and he was found to have a perforation of the anterior surface of the stomach, measuring about 1 in. (2.5 cm.) in diameter, which appeared to have completely sealed by adhesion to the anterior abdominal wall. But in view of the operative findings in the previous case and the fear that secondary leakage might result in this instance also, from later partial separation of the adhesions, it was felt wiser to break them down completely and suture the perforation. This was accordingly done, and subsequent recovery of the patient was uneventful.

Case 35.—A woman aged 72 had a two-hour history. She too failed to improve satisfactorily, and laparotomy was carried out after 24 hours of expectant treatment. She was found to have a large anterior gastric ulcer of acute type with no attempt whatsoever at localization. The perforation was sutured, but she failed to stand the strain of operation, and died 72 hours later from "peripheral failure," after her abdominal condition appeared to have settled satisfactorily.

It will be noted that all three of these patients needing secondary laparotomy were suffering from acute perforations of anterior gastric ulcers, only one of which seemed to have undergone satisfactory spontaneous closure.

Two further deaths occurred during expectant treatment.

Case 10.—A man aged 61 had a five-hour history. In addition to his abdominal catastrophe he was suffering from acute heart failure on admission and died from this cause within the next 12 hours. His general condition was such as to have contraindicated any attempt at operative surgery during the whole of this period, even had this trial of expectant measures not been in progress. Post-mortem examination showed a large acute perforation of the anterior wall of the first part of the duodenum, which appeared to have sealed satisfactorily by adhesion to the under surface of the liver. Had he lived, therefore, he might well have been a successful case of spontaneous closure.

Case 30.—A man aged 46 had a five-hour history. He was acutely shocked on admission to hospital despite his short history, and failed to recover sufficiently during the subsequent 48 hours' expectant treatment for laparotomy to be attempted. His blood pressure never rose above 70/30, and he finally died from what appeared to be primary peritoneal shock. Post-mortem examination revealed a very large anterior gastric ulcer with no attempt at localization.

Altogether, therefore, the mortality in this series of 40 cases was 10%, and the failure rate under expectant treatment was 12.5%. It is interesting that all except one of the cases of perforated duodenal ulcer recovered under expectant treatment, and that this solitary exception might also have been a successful cure had he not died from intercurrent disease. Another fact which stands out clearly is that the site of perforation in gastric ulcer has a definite bearing on the results obtained by conservative measures. It will be noticed that all three patients with lesser-curvature ulcer recovered, but that only one of the four cases of anterior perforation lived, and this only after secondary operative closure.

The single case of recovery from gastric carcinoma was probably an unusually fortunate result. Subsequent barium-meal examination a month after his discharge showed a large carcinoma which must have been inoperable at the time of perforation. This patient died within a month of readmission to hospital, and post-mortem examination showed a primary ulcerative type of gastric carcinoma on the anterior wall of the stomach. This had apparently perforated and sealed successfully, although the degree of malignant infiltration of the anterior abdominal wall made reconstruction of the previous acute pathology difficult.

Conclusions

It appears justifiable from this series of cases to draw the conclusion that the expectant method of treatment in acute perforated peptic ulcer does not give results as good as those obtained by operative surgery. Before the advent of antibiotics and other forms of chemotherapy most large series of operative results gave a mortality varying between 15 and 18%, but the figures which are available since the last war show that the inclusive mortality of surgical methods of treatment is now less than 8%. In comparison with the latter figure, the mortality of 10% in this series is not satisfactory. Were it possible to be sure of the actual site of perforation, and to treat only the duodenal and lesser-curvature ulcers by expectant measures, the method might be justifiable. But unfortunately this is not generally feasible, and the mortality rate in the expectant treatment of anterior gastric ulcers in this series has been extremely high.

As the result of my experiences, therefore, I have entirely given up the expectant method of treatment. What is now done is to carry out laparotomy in every case, as soon after admission as possible. If the perforation is found to have sealed adequately, either by adhesion to the liver or by means of an omental plug, the abdomen is closed again with no further surgical intervention and conservative treatment is then instituted. Actual operative closure of the perforation is normally reserved for cases which do not appear to be sealing spontaneously, though it is carried out routinely in every instance of anterior gastric ulcer.

Finally, it is interesting to note the high incidence of chest complications during expectant treatment. Of the 36 patients who lived, no fewer than 13 developed either localized pneumonitis or basal collapse. In 10 cases this was right-sided, in two it was on the left, and in one case it was bilateral. This is approximately the same incidence of pulmonary lesions as that following operative treatment of perforated peptic ulcer, and it appears to support the anaesthetists' contention that this complication is not primarily the result of their ministrations. It was indeed fortunate that, despite this high incidence of minor chest complications, all of them settled satisfactorily under routine chest treatment and chemotherapy, and that there was no case of subphrenic abscess or other secondary complication of such nature in this series.

Summary

The results are presented of treating expectantly 40 unselected cases of acute perforated peptic ulcer.

The cases were treated by immediate aspiration of the stomach contents, continuous gastric suction, repeated injections of morphine, and intravenous infusion. The patients were kept under constant review during the first 48 hours of expectant treatment, and laparotomy was performed if there was no obvious clinical improvement.

In this series the mortality rate was 10%, and the failure rate with expectant treatment was 12.5%. Thirty-one cases out of 32 with perforated duodenal ulcers recovered under expectant treatment, but only one out of four cases with anterior perforations of the stomach survived. There was a high incidence of chest complications during treatment.

The expectant method of treatment has now been abandoned in favour of early laparotomy in every case.

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SIGNIFICANCE OF RAISED SERUM-ENZYME LEVELS IN PERFORATED PEPTIC ULCER

BY

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Aside from renal considerations, a rise in the amylase content of the blood or urine is generally regarded as an indication of some form of damage to the exocrine system of the pancreas. The gross and the microscopical pathological changes may conform to one of the recognized types of acute pancreatitis or may be so slight as to be imperceptible: instances of the latter have been recorded in which presumably the duct of Wirsung has been affected by the presence of gallstones or of some other agency such as a T-tube left in the common duct for drainage (Millbourn, 1936; Lewison, 1941). In others, a chronic duodenal ulcer burrowing into the pancreas is the disturbing factor (Probstein, Wheeler, and Gray, 1939).

There is experimental evidence to show that the amylase, after its escape from damaged acini or ducts, finds its way into the peripheral blood mainly via the portal system: lymphatic absorption plays a secondary part (Popper and Necheles, 1940; Howard, Smith, and Peters, 1949). It would now appear that a free perforation of a gastric or duodenal ulcer has some claim to be regarded as one of the conditions likely to cause the blood or urine amylase levels to rise. Mikkelsen (1934) cited instances from his own experience in which this complication was associated with hyperdiastasuria, but gave no details of the incidence or significance of this finding.

The first large-scale study of the problem was carried out by Hughes (1942). He investigated 40 patients with perforation of a gastric or duodenal ulcer and found four with a urinary diastatic index of the order of 300. I studied the concurrent amylase and lipase changes in the blood in a series of 30 perforated cases, in none of which was the pancreas involved by ulcer (Wapshaw, 1949). Slight deviations from the normal standards were noted in four and substantially raised values in two cases. High though the latter were, they fell short of the values obtained in two cases of acute pancreatitis which were comparable in respect of the duration of illness. Musgrove (1950) has recently added three more to the list, apparently the first to be reported from the Mayo Clinic. One was a perforated reticulum-cell sarcoma; the other two were ordinary perforated peptic ulcers.

The aetiological significance of the increases in enzyme content of the blood or urine is still uncertain. Hughes suggested that they might be due to (1) an overlooked patch of acute pancreatitis; (2) a second peptic ulcer lying posteriorly and adherent to the pancreas; or (3) transperitoneal absorption of the pancreatic ferments contained in the gastric or intestinal contents which had passed into the abdominal cavity. Neither of the first two probabilities was confirmed in the cases which were examined post mortem.

A group of workers at the Mayo Clinic—Pemberton, Grindlay, and Bollman (1950)—stimulated by Musgrove's findings, carried out what seems to be the first experimental attempt to trace the source of the surplus amylase. Not only did they duplicate in dogs the conditions in humans, but they were also able to define the perforations both in time and in location. A decided rise in the serum amylase was observed in animals which suffered perforation within one to two hours after a full meal—that is to say, when the pancreas was secreting to full capacity. If the perforation was delayed for three to four hours the amylase levels in the blood were unaffected. In samples of the peritoneal fluid withdrawn by abdominal paracentesis the amylase concentration of the early group was about six times that of the later. The mortality from peritonitis was very high, particularly among animals belonging to the former group, but, according to the control experiments, peritonitis cannot be held responsible for the hyperenzymaemia. Pemberton *et al.* concluded that the determining factor was the amylase concentration of the free fluid in the abdomen.

In the course of previous clinical study I independently accumulated data bearing on points studied by the Mayo Clinic team, such as the times of the previous meal and the enzyme activity of the fluid inside the abdominal cavity encountered at operation. It seems of value to place these findings on record. The results are further amplified by the inclusion of repeat serum-enzyme observations which were made in most of the patients 24 hours after the initial readings.

Findings in 32 Perforation Cases

Pathological Data

It must be emphasized again that in none of the cases had the ulcer process implicated the pancreas. The site-incidence of the perforations was as follows: pyloro-duodenal, 29; gastric, 2; anastomotic, 1. Simple closure was carried out on 28 patients, with one death. Two patients were admitted to hospital with widespread peritonitis and died soon after (Cases 1 and 27). There were also two late cases which had developed subhepatic abscesses when first seen; both made a good recovery following open drainage (Cases 31 and 32).

In Case 27, at necropsy, a second ulcer was found lying posteriorly and loosely adherent to the pancreas. A few spots of fat necrosis were also observed in the fatty tissue of the lesser and greater omenta of this case. Yet the parenchyma of the gland appeared normal on section, and certainly the enzyme findings in the blood gave no reason for one to think otherwise.

Enzyme Findings in the Blood

Amylase and lipase estimations were carried out with the same sample of blood. In the former, the Somogyi iodometric test was employed. The normal values range between 70 and 200 units per ml. of serum. For

determining the lipase activity the Cherry and Crandall method was used. Normal values do not exceed 1.5 ml. of N/20 NaOH per ml. of blood serum.

The patients were investigated soon after admission to hospital; in 15 of the operated cases the tests were repeated 24 hours later so as not to miss any late enzyme variations. The results are given in the Table. The following summarizes the chief findings.

Initial Readings.—The highest abnormal values for both enzymes were found in a case of two days' standing too ill with peritonitis to be saved by surgery (Case 1). Another with considerably raised readings was a 15-hour perforation (Case 3); this patient also died from peritonitis. Cases 8, 11, 13, and 14 had slightly raised amylase readings. An associated rise in the lipase levels was noted in Cases 13 and 14. These cases all fell within the group which had been ill for 7 to 12½ hours when first examined. The findings in all those seen earlier than the seventh hour were normal, as were also the findings in the two late cases complicated by abscess formation (Cases 31 and 32).

Findings in 32 Cases of Perforated Peptic Ulcer in Order of Duration of Illness. Repeat Serum-enzyme Estimations were Carried Out 24 Hours Later

Case No.	Site of Perforation	Duration of Illness Before Study (hrs.)	Time of Perforation Since Previous Meal (hrs.)	Serum		Peritoneal Fluid	
				Amylase (Somogyi Units) (Normal 70–200)	Lipase (ml. N/20 NaOH) (Normal 0–1·5)	Amylase (Somogyi Units)	Lipase (ml. N/20 (NaOH)
12	Stomach	2½		160			
5	Duodenum	2½	5	46	0·0	94	0·5
2	,,	3		177	0·3		
26	Pylorus	3		145			
28	Duodenum	4	7		0·1		12·3
					1·0		
9	,,	4	2	145	0·2	0	0·1
				190	0·9		
29	Pylorus	4	4½		0·6		6·4
					0·8		
15	Duodenum	4	¼	53	0·1	200	9·0
7	,,	4½	During meal	184	0·4	6,400	11·4
				84	0·4		
16	Stomach	5	4	133	0·7	3,200	9·2
21	Duodenum	5	3	76	0·3	400	10·2
4	,,	6	6	65	0·1		
10	,,	6	6	84	0·0		
				56	0·1		
18	,,	7	4	88	0·1	710	7·5
				84	0·2		
17	,,	7	2	66	0·7	800	4·9
				80	0·5		
14	,,	7	5	355*	1·7†	32,000	14·3
				355*	0·1		
30	,,	7	¼		0·4		4·8
25	,,	7	4	168	0·1		
				200	0·3		
23	,,	7		106	1·5	133	0·3
22	,,	8	5	106	0·7	9,600	10·0
20	Anastomotic ulcer	9	4	106	0·8	400	0·5
11	Duodenum	9	6½	266*	0·2	6,400	13·0
				80	0·0		
8	,,	10½	6	248*	0·75	13,330	14·0
				80	0·85		
6	,,	11	4	66	0·1		
				123	0·1		
13	,,	11	3	266*	2·1†		
				180	0·55		
19	,,	12	5	88	0·0	1,770	4·3
				106	0·8		
24	Pylorus	12½	5	88	1·3	3,200	6·5
				300	1·4		
				22‡	0·66‡		
3	Duodenum	15 (died)		640*	2·5†	48	8·0
27	,,	24 ,,		177	0·7		
1	,,	48 ,,		720*	4·1†	1,600	7·0
31	,,	10 days		73	0·4		
32	,,	18 ,,		106	0·3		

* Raised serum-amylase readings. † Raised serum-lipase readings. ‡ Result at 48 hours.

Repeat Readings.—The results obtained on re-examination 24 hours later did not conform to any definite pattern, nor did such changes as were noted in the amylase and lipase concentrations always run parallel. It is noteworthy that the second readings in the four cases which had originally a moderate increase in the serum amylase were within normal limits except in Case 14, which remained elevated. A drop to normal levels also occurred in the two with moderately raised lipase values. In nine others there was no appreciable difference between the first and second readings. In the remaining two cases (Cases 6 and 24) the second amylase reading was decidedly raised, though in Case 6 it was within normal limits.

Enzyme Concentration of the Peritoneal Fluid

This was examined in 21 cases. The samples were obtained at operation in all except the first in the series, in which recourse was had to paracentesis abdominis ante-mortem. The same two tests were employed as mentioned above. If dilution was required, sterile physiological saline was used.

The results varied between wide limits. For example, the amylase concentration ranged from zero in Case 9 to 32,000 units in Case 14, and the lipase from 0.1 ml. in Case 9 to 14.3 ml. of N/20 NaOH in Case 14. A comparison between those findings and the corresponding results with the blood serum failed to show any correlation such as would lead one to suppose that the concentrations in the latter were augmented from a peritoneal source. It is conceivable that an excess of pancreatic ferments had been carried from the peritoneal cavity into the blood in Case 14, but in the light of the other findings this evidence must be regarded as purely circumstantial.

Time Since Previous Meal

This was noted in 23 cases. One patient perforated during a meal, four within two hours, and in the remainder the lapse of time was three or more hours, the average being four hours.

It was thought at first that the data might give some indication of the functional state of the pancreas at the time when the leakage of the gastric or duodenal contents occurred. However, the results of the estimations carried out on the fluid from the abdominal cavity gave little support to this assumption. Actually the highest concentrations were found among those who had not eaten food for several hours. Nor was there any relationship in respect of time with the findings in the blood serum such as has been reported by Pemberton and his associates.

Discussion

The question at issue is whether or not the changes in enzyme content that have been observed in the blood and urine in certain perforation cases denote a genuine disturbance of the pancreas. It is true that fat necrosis was encountered both by Hughes and by me in patients showing abnormally high readings, but further exploration ruled out a co-existing pancreatitis. The fat necrosis was doubtless the effect of a lipase of high potency which had obtained access to the peritoneal cavity as a result of the perforation. It is difficult, however, to ignore the possibility that the pancreas is sometimes functionally deranged either at the time of perforation or later. The irritant nature of the escaping fluid, particularly when it has become infected, might conceivably lead to changes in the exposed parts of the gland, though parenchymatous changes such as round-cell infiltration or interstitial oedema have not been noted in the deeper parts.

Pemberton and his colleagues were induced to consider this possibility in the course of their studies. By way of a control experiment, they produced a virulent and rapidly fatal peritonitis by the intra-abdominal injections of faecal and other noxious matter, but without

obvious effect on the amylase levels in the blood. It is fair criticism that their experimental conditions did not strictly parallel the clinical, for, whereas the dogs so treated died in the space of four hours, the present investigation leads one to believe that in clinical cases the enzyme levels become materially raised, if at all, only at a later stage. Thus it was found that the cases with abnormal readings had been perforated for a period of 7 to 48 hours; and Musgrove's cases were of one, four, and six days' standing.

When the problem presents itself for the first time after operative intervention, other factors have to be considered, such as the amount of traction required to expose the lesion and even the anaesthetic administered. In regard to the latter, ether is perhaps the drug which calls for the closest attention. Its effects have been studied in animals and the reports are conflicting. Some state that the inhalation of ether has a negligible effect on the serum amylase (Watanabe, 1918; Ross and Davis, 1921), while others believe that it results in a slight increase in concentration (Karsner, Koeckert, and Wahl, 1921; Zucker, Newburger, and Berg, 1932). Lewison refers to the occasional occurrence of abnormal readings after laparotomy, which some allege are due either to the anaesthetic or to intra-abdominal manipulations, but he himself has been unable to substantiate these explanations. With regard to the effects of mechanical trauma, it would seem that the pancreas does not object to gentle handling, but if subjected to damaging injury it registers its protest in the form of a serum-amylase response of moderate degree (McCaughan, 1934).

The experimental evidence brought forward in support of the theory of transperitoneal absorption is convincing. The effect produced by the entry of pancreatic ferments into the blood stream will depend, among other things, on the amount and potency of the secretion of the pancreas at the time of perforation. It was with a view to finding out something of this aspect of the problem that note was taken of the times of the previous meal. The findings suggested that a peptic ulcer is apt to perforate during the interdigestive phases of gastric and pancreatic secretion. The same impression is conveyed by Illingworth, Scott, and Jamieson (1944) in their statistical study of 951 perforations treated at the Glasgow Western Infirmary during 1938–43 when they state that the incidence was highest between 3 p.m. and 6 p.m.—that is, towards the end of the ordinary working day. It is of interest, however, that Strang and Spencer (1950), at Newcastle-upon-Tyne, were unable to correlate the time of occurrence with any particular phase of digestion.

The intraperitoneal findings in the perforation series were inconclusive. So far as could be determined from the data relating to the previous meal, there was no correspondence between the enzyme activity of the free fluid in the abdomen and the different phases of pancreatic function, nor was there any apparent connexion with the enzyme levels in the blood. One hesitates to infer that the possibility of absorption via the peritoneal lining is ruled out on that account. The diversity of the readings may have been due to factors that are beyond analysis clinically; for example, the secretory response evoked by the preceding meal, the degree of enzyme inactivation that is apt to result from an admixture with the acid chyme of the stomach, and the diluent effect of the peritoneal exudate are but a few of the incalculable variables which have to be taken into account.

Summary

Slight increases in the amylase and lipase levels in the blood occur in a small minority of peptic ulcer cases complicated by perforation.

No histological cause for these changes has been found in the pancreas.

A study of the clinical data in the present cases failed to yield evidence either for or against the view, supported by experimental work of others, that the increase in blood levels of the enzymes is due to their absorption into the circulation from the abdominal cavity.

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ADDENDUM.—Since this paper was written another case with raised readings has come to notice. The findings were: male, aged 37; anterior duodenal perforation of 22 hours' duration; serum amylase, 400 Somogyi units; peritoneal fluid amylase, 1,140 Somogyi units; meal one hour before onset of symptoms; recovered after operation.

Medical Memorandum

Persistent Bacillary Dysentery Carrier Treated with Chloramphenicol

Bacillary dysentery is endemic in many mental hospitals, carriers being the main source of infection (Medical Research Council, 1929). Our recent successful treatment of a persistent dysentery carrier with chloramphenicol is felt to be of general interest. The patient had previously remained resistant to sulphonamide therapy during a period of 19 months.

Case Report

In September, 1948, a small outbreak of bacillary dysentery occurred in a female mental ward of approximately 50 patients. There were three clinical cases, and the administration of sulphaguanidine resulted in a prompt cure.

Two months later, on November 5, 1948, the stools of all the patients in the ward were tested and five symptomless carriers were discovered. The infecting organism, both in the carriers and in the previously treated clinical cases, proved to be *Shigella flexneri* (variant X type). Four of the carriers were successfully treated with sulphaguanidine, but the fifth proved resistant. This was a woman aged 28 who had been in an institution since 1936 without previous history of clinical or bacteriological dysentery. She had no general symptoms when examined, and her stools were

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normally formed, with absence of either blood or mucus. A standard course of sulphaguanidine was administered, 6 g. four-hourly to a total of 130 g. over seven days, but her stools remained positive.

The patient received the treatment shown in the Table.

Date	Treatment	Total Dose	Result	Relapsed
10/1/49	Sulphaguanidine	130 g.	3 negative stools over 3 days	21/1/49
1/2/49	Sulphathiazole	29 g.	No effect; stools remained positive	
2/3/49	Sulphaguanidine for 10 days plus daily pot. permang. enemas	186 g.	No effect; stools intermittently positive	
15/2/50	Sulphadimidine	86 g.	3 consecutive negative stools over 22 days	27/3/50
29/3/50	Sulphadiazine	72 g.	4 consecutive negative stools over 10 days	24/4/50
24/4/50	Sulphadimidine	63 g.	3 consecutive negative stools over 18 days	22/5/50

From April, 1949, to January, 1950, no active treatment was carried out, 28 stool examinations being made, of which 22 were positive. An agglutination test carried out in November, 1949, using the patient's serum against standard flexner cultures and flexner bacillus isolated, gave a negative reaction in a dilution of 1/25.

In January, 1950, the Public Health Laboratory, Leicester, kindly carried out sensitivity tests on the organism and found it to be resistant to succinylsulphathiazole and only weakly sensitive to phthalylthiazole and sulphaguanidine. It was, however, shown to be sensitive to sulphadimidine, sulphadiazine, sulphamerazine, and sulphanilamide. In addition it was found to be sensitive to 5 units of streptomycin per ml. and to 25 μg. of chloramphenicol per ml.

Further sulphonamide therapy was then given in 1950 (see Table).

From May 22 to June 2, 1950, six stools were examined, five of which were positive. At the beginning of June, thanks to the co-operation of the Ministry of Health and the City General Hospital, Nottingham, 12 g. of chloramphenicol was obtained, being administered over the course of five days (June 2–6). The initial dose was 750 mg.; this was followed by 250 mg. two-hourly for one day and then 250 mg. three-hourly for the remaining four days.

In the 50 days immediately following completion of treatment, 29 consecutive negative stools were obtained. The stools were still consistently negative four months after completion of treatment.

During the period in which the patient was a known carrier (19 months) 66 stools were examined and 39 (60%) of the specimens were positive. Colonies varied during positive periods from 10 to 117 per plate on desoxycholate citrate media. The patient remained entirely free from symptoms during the whole period.

Comment

Chloramphenicol has been shown to be active *in vitro* against *Shigella paradysenteriae* (Sonne) amongst other Gram-positive and Gram-negative bacilli (Smith *et al.*, 1948). Ley and his co-workers (1948), when determining blood and urine levels after oral administration, used a microbiological assay involving the inhibition of the growth of *Shigella paradysenteriae* (Sonne).

There have been two recent reports on the clinical use of chloramphenicol in acute bacillary dysentery. Mazursky (1950) describes the treatment of three acute cases of Sonne dysentery and claims good results. He found a rapid change in the character of the stools, but unfortunately a long-term follow-up was not possible. Ross *et al.* (1950) treated 35 children with shigella enteritis and found that their results compared very favourably with similar series previously treated by them with sulphadiazine, streptomycin, and polymyxin B.

So far as we are aware this is the first published account of the use of chloramphenicol in the treatment of a chronic bacillary dysentery carrier. Chloramphenicol was found to be active both *in vitro* and *in vivo*. The absorbable sulphonamides—sulphadiazine and sulphadimidine — although apparently active *in vitro*, had only temporary effects when used clinically. Sulphaguanidine was only slightly active *in vitro*, and the possibility arises that initial treatment led to subsequent resistance to the drug. All three clinical cases and the four other carriers isolated about the same time had responded promptly to one course of sulphaguanidine.

It is well known that carriers may excrete bacilli intermittently, and serial stool examination is thus essential when assessing the efficacy of treatment in a dysentery carrier. In our case it was very uncommon to find more than two consecutively negative stools except after courses of treatment. Four consecutive negative stools were obtained after a course of sulphadiazine and three consecutive negative stools were obtained after courses of sulphadimidine and sulphaguanidine.

In conclusion, it may be said that, though the efficacy of a particular drug cannot be established by the treatment of one case, the result obtained has been sufficiently prompt and clear-cut to warrant further investigation.

We wish to acknowledge our thanks to Dr. K. K. Drury for permission to publish and for advice, to Dr. A. B. Monro for advice and criticism in the preparation of this memorandum, and to Mr. F. Mills and Mr. J. A. Scott for their valuable laboratory work.

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The *Annual Report for 1950* of the Health Branch of the Government of British Columbia notes that there has been a marked drop in both the mortality and morbidity of tuberculosis during the year. Nearly 80,000 people were *x*-rayed in clinics. B.C.G. is being offered to all contact children with negative tuberculin reactions. The control of venereal disease also seems to be successful, since there were only 62 cases of syphilis during the year, the lowest figure ever recorded, in spite of the fact that half of the 1,138,000 people of British Columbia live close to a major seaport. Two diagnostic programmes are of interest. A special centre exists in the Vancouver City Gaol, and out of 2,800 prisoners examined during 1950 5.5% revealed hitherto undiscovered venereal disease. These centres are to be opened in other prisons. A blood-testing survey among Indians employed in canneries also proved a successful method of case-finding among a selected group. It is interesting to note that penicillin is issued free of charge to private practitioners on notification of a case of venereal disease, and cases of gonorrhoea are treated with 500,000 units of penicillin in the hope of eliminating hidden syphilis.

Reviews

BACTERIAL POLYSACCHARIDES

Bacterial Polysaccharides. By M. Burger. (Pp. 272. 45s.) Oxford: Blackwell Scientific Publications. 1950.

This book contains a useful historical survey of the investigations which have led up to our present knowledge of the chemical and immunological properties of the polysaccharides associated with the more common types of pathogenic bacteria. In a space of 254 pages the author discusses in a fairly comprehensive manner the isolation and properties of those polysaccharides which are considered to play an important part in infection and immunity. There are inevitable gaps in the contents because the author does not encroach unduly on the closely related subject of bacterial antigens, and it is presumably for this reason that the excellent work of Miles and Pirie on the components of the antigenic complexes of *Br. abortus* and *Br. melitensis* receives only passing reference and Chargaff's work on Proteus OX 19 is omitted. Nevertheless the book contains a large amount of useful information, simply and clearly set out, which covers the chemical properties of the immunologically important polysaccharides of bacteria. A useful chapter on the enzymic decomposition of certain polysaccharides and on the effect of enzymes on experimental pneumococcus infections is included. The inclusion of a fairly detailed account of the preparation and properties of the bactericidal agents gramicidin and tyrocidine comes as a surprise in a book on bacterial polysaccharides.

It is unfortunate that all but one of the practical methods given in the Appendix for the preparation of bacterial polysaccharides are more than 10 years old and that none involves the use of high-speed differential centrifugation or suggests control of the homogeneity of the product by analytical procedures, such as electrophoresis or ultracentrifugation, which have been in fairly general use for the last decade.

The book is well produced, has many tables which bring together much useful information, and is a valuable addition to those already available in the field. It will be of considerable use to immunologists and those engaged in the study of immunochemistry.

W. T. J. MORGAN.

DISCUSSIONS ON ENDOCRINOLOGY

Transactions of the American Goiter Association, 1949. (Pp. 460; illustrated. £3 17s. 6d.) Springfield: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1950.

Adrenal Cortex. Transactions of the First Conference, 1949. Edited by Elaine P. Ralli. (Pp. 189. $2.) New York: Josiah Macy, jun., Foundation. 1950.

Many of us are conscious of the fact that we have learned far more about our subjects in pubs and clubs than in the halls of learned societies, in the bars conveniently provided at international congresses than in the lecture halls. One only has to sit at the back of a lecture hall to realize how large a proportion of the audience sleep quietly through each paper, to be galvanized into mental activity when the discussion begins. There is something about the formal paper which inhibits attention: it may be the realization that it will be far more profitable to read it later by one's own fireside, especially if the lecturer's delivery is as bad as it usually is. Some of us may have thought it a pity that the paper shortage, which has done so much to increase the lucidity of British scientific papers, should have made it impossible to publish discussions. When, rarely, such discussions are published at all, they are usually polished out of all resemblance to their originals and robbed of that spontaneity which gave them their original value.

They do these things better in the U.S.A. Most of the papers in the *Transactions* of the American Goiter Association have already appeared in the *Journal of Clinical Endocrinology*. They are valuable, serious, but almost completely unreadable additions to knowledge. The serious student will no doubt have to refer to them often for some years to come. Few of them can be read with enthusiasm except in relation to the work which the individual reader happens to be doing at the particular moment of his reading. But when he has read each paper his mind changes gear. The verbatim discussion suddenly enlivens the theme, makes it human, and gives it immediate impact. You get the feeling that you never get in reading serious journals, that here are live men, lively, interested, talking intimately of things they know. There is always the danger, if this habit spreads, that the spontaneity may be lost: people may begin to talk with an eye to what will be printed. In these two books this back-sliding has not yet begun. The dead word of the scientific journal has succeeded in becoming alive through such apparently facetious comments as that by Professor Means, "When you give dinitrophenol it is like taking the clutch out of a car; the engine races, heat is produced, but nothing happens. When you give thyroxine, on the other hand, it is like stepping on the gas; the engine goes faster and the car goes ahead." And by Dr. Soley in answer to the question, "Would you treat a close relative with Graves's disease with ^{131}I?" "I would, but I wouldn't tell Dr. Rawson about it." And later, apropos of the future of treatment with ^{131}I, "Dr. Means, would you mind commenting on that question, too? We can't get Dr. Soley interested in committing himself." And the devastating question by Means on nomenclature in thyrotoxicosis, which we have all asked, but never in print, "What is what primary to or secondary to?" And Dr. Frazell's retort to another interruption, "I do not think one can get emotional about scarring up a beautiful young girl's neck when one is dealing with cancer of the thyroid."

The second book goes even further. There are no solemn set papers. The fun begins at once. Indeed, "The Adrenal Cortex" belongs to the same class of literature as the plays of Bernard Shaw. Occasionally a very important character is allowed to develop a theme for as long as a page, but after that he is subjected to almost constant interruption. Most of the characters have only a sentence or two to say at a time, but the meaning goes on in a continuous stream on which one is carried with none of that effort of concentration which the reading of the average textbook needs. These discussions are so informal and intimate that one almost feels that one is present at this learned but never heavy or pompous conversation. The illusion would be enhanced if Josiah Macy would borrow an idea from Charles Thomas and give us photographs of the dramatis personae.

RAYMOND GREENE.

HISTORY OF THE INDIAN MEDICAL SERVICE

Surgeons Twoe and a Barber. Being Some Account of the Life and Work of the Indian Medical Service (1600–1947). Compiled and furnished with an introductory essay by Donald McDonald. With foreword by Lieutenant-General Sir Bennett Hance, K.C.I.E., O.B.E., K.H.S., L.M.S. (Pp. 295; illustrated. £2 2s.) London: William Heinemann. 1950.

In this pleasantly produced and handsomely illustrated book the author gives an account of the Indian Medical Service. A history of the service by D. G. Crawford was published in 1914, but the present account is less a formal history than a story of the life and work of the service. While it describes its formation and growth from the time when, as may be gathered from the title, a surgeon and a barber were of much the same standing, it carries the story through two world wars to August 15, 1947, when with the transfer of power to the two Dominions of India and Pakistan the Indian Medical Service ceased to exist. To any member of the service now living the book will revive many memories, but it will be interesting also to others, for in a sense the history described is a microcosm of life and work under British rule in India and all that went with this.

After an introductory foreword by Sir Bennett Hance, Director-General in 1943–6, who refers to the desirability that the story of the I.M.S. should be made more popularly available, the book goes on to describe the origin of the service in what were truly adventurous times to the establishment of what has been one of the most remarkable medical services ever to come into being, one not only famous for its contributions to research in tropical medicine, but unique in the scope of its many activities. The book gives a full and interesting account of how, and by whom, were developed the great medical and public health institutions which exist throughout India, the dispensaries and hospitals, the arrangements for medical education, the triumphs of medical research, the part played by officers of the service in many theatres in the two world wars, and much else. There is a special chapter on the I.M.S. and medical research by Lieutenant-Colonel H. W. Mulligan, I.M.S., one on the I.M.S. and public health by Lieutenant-Colonel C. A. Bosman, I.M.S., and others on medical education and on the subordinate medical services in India. The text is accompanied by some excellent photographs, including those of some former Directors-General. Members of the service will greatly appreciate such a well-conceived and ably carried out tribute to a service of which all are justly proud, and others will find much about India of interest.

S. R. CHRISTOPHERS.

STERILIZATION

Sterilization in North Carolina. A Sociological and Psychological Study. By Moya Woodside. (Pp. 219. £1.) London: Geoffrey Cumberlege. 1950.

Twenty-seven of the 48 States comprising the U.S.A. have laws which provide for compulsory sterilization for eugenic and social reasons, the first of these having been enacted in 1907. North Carolina has a largely rural community of rather less than four million, of which approximately one-quarter is negro. A sterilization law was introduced there in 1929, but in 1933 it was replaced by another which offered better protection to the rights of the individual. The law is not concerned with sterilization for medical indications but with the operation as carried out at the instigation of institutions dealing with mental disorders and delinquency, and of certain public health bodies in cases of feeble-mindedness, mental disease, and epilepsy. About 140 operations are performed under these headings each year in North Carolina, more than two-thirds of them on women.

The author of this book, a psychiatric social worker from Britain, gives an "outsider's view" of the development of this social experiment and its results, and indirectly presents the case for and against eugenic sterilization. As it applies in North Carolina it evidently aims more at reducing immediate social and economic problems than at improving the quality of the future population. Many professions will be interested in Mrs. Woodside's findings and observations. From the strictly medical point of view one of the most valuable sections is the account of a follow-up of 48 women previously sterilized by bilateral tubal ligation or resection. In general it was found that the operation conveyed definite physical and psychological benefits and was without significant effect on the sexual life or feelings of individuals.

In North Carolina it is clear that the sterilization law is limited in scope and that the compulsion clauses are rarely applied—sterilization being carried out by persuasion rather than force. Nevertheless, it has its pitfalls and problems as well as advantages, and the experience reported here should be known to all those who have in mind the introduction of this type of legislation elsewhere.

T. N. A. JEFFCOATE.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Dementia Praecox or the Group of Schizophrenias. By E. Bleuler. (Pp. 548. 63s.) London: George Allen and Unwin. 1951.

The Faithless Lover and Other Poems. By L. Ley. (Pp. 64. 6s.) Norwich: Jarrold. 1950.

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BRITISH MEDICAL JOURNAL
LONDON
SATURDAY MAY 5 1951

MEN AND MACHINES

The proposition that working conditions can be more easily altered than human anatomy and physiology is of such obvious truth that it might have been thought unnecessary to found a society, or to hold a conference, to call attention to it. Shoes should fit feet, railway upholstery should fit backs, and baths should hold their occupants. Yet it is only within the last few years that a system of shoe-fittings has been devised which is based on the statistical analysis of foot measurements; railway seats are found almost universally uncomfortable by those who attempt to sleep sitting up; and pocket-sized baths seem to have been accepted as a necessary concomitant of pocket-sized flats. It is hardly surprising in the circumstances that the design of industrial equipment, seating, work-spaces, and general lay-out should have received little attention as yet, except in the obvious sense that controls are placed in positions which to their designers appear reasonable, and that economy of material-movement in factories is an accepted principle. What has yet to be recognized on any general scale is that efficiency as well as comfort may be promoted by fitting the machine to man, and that biological research at the design stage may often be needed to obtain the best fit possible. There is in these facts the justification of the Ergonomics Research Society—including the addition of one more name to those found in the literature—and of the symposium which has been held lately by the Society at Birmingham on "Human Factors in Equipment Design." It is a subject on which wartime experience should prove of value. An anatomist's response was quoted by Le Gros Clark in 1947. His example was the design of sighting equipment so pivoted as to enable the observer to follow aircraft movements as naturally as possible; and his conclusion was that it was necessary, or at least useful, to begin by studying composite movements through records made as a film, before proceeding to either detailed analysis or the giving of advice. The applied physiology of aviation and cockpit design is a more widely known example. Ergonomics has been defined broadly as the study of the relationship between man and his working environment. It includes, therefore, the effects of climate; and it may be recalled that the Linen Industry Research Association has lately found it possible to recommend modifications in the local climate of certain "wet" processes to the advantage of the worker and without technical loss.

The dimensions of the worker appear as an essential but unalterable factor in many problems. At the Birmingham symposium, Clements took up two points of very general significance: the question of distinctive population groups, and the derivation of the special measurements wanted for equipment design from weight and height statistics, which are more readily available. On the first he concludes that regional differences are largely mythical, but that the Registrar-General's classification of the population by social groups is significant for anthropometry. On the second problem he thought that the required special measurements could be obtained by their empirical relation to weight and height. Morant, going a step further, has considered the space occupied by people of known dimensions in different positions. Akerblom, in Sweden, has returned to the vexed question of seating, and Christensen has applied physiological arguments based on the effects of physical work on the circulation with the body in different positions. Muscular activity has been studied in a variety of conditions by Floyd and Silver, using the methods of electromyography, and the normal movements of the spine and of stretching have been investigated by Darcus. Psychological considerations enter particularly into the design and placing of indicator dials and control mechanisms, and in both Great Britain and the United States[1] there is much research now in progress on these aspects. It would be premature, in almost any respect, to suggest that knowledge of the underlying biological problems is complete, or nearly so; only a beginning has been made. But the view is reasonable which was expressed by Sir Ben Lockspeiser, in his opening address to the symposium, that "enough is known to justify the introduction of biological considerations as a distinctive contribution to machine design," and that this should be "at the earliest stages of preliminary design, prototyping, and field trial, when, if necessary, radical changes of design are economically possible."

[1] Symposium on Human Engineering, *Ann. N.Y. Acad. Sci.*, 1951, **51**, 1123.

ALLERGIC ENCEPHALOMYELITIS

The febrile neurological complications of vaccination against smallpox, rare at the beginning of this century, became much commoner during the third decade, and for 1928 the Registrar-General reported 55 cases of post-vaccinal encephalomyelitis in England and Wales. The incidence has since fallen, though there has been no corresponding decrease in the number of vaccinations performed. On epidemiological grounds it was at first thought that infection with vaccinia had stimulated into activity a latent neurotropic virus, possibly that of encephalitis lethargica. But the crescendo in the incidence of post-vaccinal encephalomyelitis coincided with the decline of the encephalitis lethargica epidemic, and the two diseases are not only clinically but also histologically distinct.

Although allergy as the basis of the nervous complications of vaccination, smallpox, and chicken-pox was first suggested in 1927 by Glanzmann,[1] recent experimental work on the subject is based on much earlier studies on the toxicity of anti-rabies vaccine, which is an emulsion of the cord of a rabid animal. Thus wasting, convulsions, paralyses, and sterile abscesses at the site of injection occurred after the administration of normal as well as rabid brain emulsion to rabbits, and injection of heterologous nervous tissue led to the formation of sera with neurotoxic properties *in vivo*. On such evidence Harvey and McKendrick[2] suggested in 1907 that "anaphylaxia due to foreign nerve substance" was the cause of the paralytic accidents after rabies vaccination. Later Brandt, Guth, and Müller[3] obtained complement-fixing antibodies to brain tissue by injecting alcoholic extract of homologous brain (of the same species as the injected animal) mixed with a heterologous protein "conveyer" (from a different species), thus demonstrating the presence of a lipoid haptene (determining antibody specificity) in nervous tissue. Even so, there was no evidence that such antibodies in sera were responsible for the neurotoxic effect of the latter, nor that the lesions produced by the sera resembled those in the myelitis occurring after anti-rabies vaccination. Plaut and Kassowitz[4] saw no abnormalities in rabbits injected intracerebrally (across the blood–brain barrier) with serum containing brain-specific antibodies. Conversely, Weichsel and Salfeld[5] failed to detect antibodies to brain in the sera of persons receiving vaccines prepared from nervous tissue.

In 1928 Perdrau[6] linked up this experimental work with post-vaccinal encephalomyelitis and laid the foundation for the present-day investigations. He showed that perivascular demyelination was the earliest detectable lesion in both post-vaccinal encephalomyelitis and myelitis after inoculation against rabies. Five years later Rivers and his colleagues[7] observed lesions resembling post-vaccinal encephalomyelitis in monkeys after administering many alternate injections of alcoholic extract and aqueous emulsion of rabbit brain. Schwentker and Rivers[8] further showed that brain-specific antibodies appeared after injections of autolysed or vaccinia-infected homologous brain tissue without conveyer. This suggested that post-vaccinal encephalomyelitis might result from the production of auto-antibodies in response to damaged nervous tissue in the same animal. Kopeloff and Kopeloff,[9] applying Freund and McDermott's[10] "adjuvant" technique, obtained brain-specific antibodies in monkeys. In this the "antigen" in aqueous phase is suspended in a lanolin-like base, which is then mixed with a suspension of killed tubercle bacilli in paraffin oil. Kabat and his colleagues[11] and Morgan[12] observed perivascular, demyelinating lesions in monkeys in less than a month after only one injection of this antigen. A similar result has been obtained in guinea-pigs.[13] The efficacy of this adjuvant technique is thought to depend on the fact that antibody-producing cells are attracted by the tubercle bacilli and thus come close to the "antigen," and Kabat and his colleagues[14] have shown that the encephalitic lesions which are associated with antibody production appear more quickly only when the injection of brain emulsion is given at the same site as the tubercle bacilli. However, this does not indicate a causal connexion between the antibodies and the lesions, any more than between the tissue antibodies taking part in the Wassermann reaction and the lesions of syphilis. The recently demonstrated efficacy of non-lipoid residues and other indications of the protein nature of the encephalitogenic agent contrast with the lipoid character of the haptene responsible for antibody production. Again, Schwentker and Rivers[8] showed a relationship between antibody production and the myelin content of the emulsion injected, whereas Lumsden[15] found non-myelinated (foetal) nervous tissue fully encephalitogenic. Failure to transmit the experimental disease by transfusion or cellular transfer is evidence against the importance of

1 *Schweiz. med. Wschr.*, 1927, **57**, 145.
2 *Scientific Memoirs of the Government of India*, 1907, No. 30. Calcutta.
3 *Klin. Wschr.*, 1926, **5**, 655.
4 *Z. ImmunForsch.*, 1929, **63**, 428.
5 *J. Immunol.*, 1936, **31**, 421.
6 *J. Path. Bact.*, 1928, **31**, 17.
7 *J. exp. Med.*, 1933, **58**, 39.
8 Ibid., 1934, **60**, 559.
9 *J. Immunol.*, 1944, **48**, 297.
10 *Proc. Soc. exp. Biol., N.Y.*, 1942, **49**, 548.
11 *J. exp. Med.*, 1947, **85**, 117.
12 Ibid., 1947, **85**, 131.
13 Freund, J., Stern, E. R., and Pisani, T. M., *J. Immunol.*, 1947, **57**, 179.
14 *J. exp. Med.*, 1948, **88**, 417.
15 *Brain*, 1949, **72**, 517.
16 Ibid., 1949, **72**, 198.
17 Marsden, J. P., and Hurst, E. W., *Brain*, 1932, **55**, 181.
18 Hurst, E. W., *Med. J. Aust.*, 1941, **2**, 1.

antibodies. However, Lumsden's[16] demonstration that antihistamine drugs have a protective effect—which he cautiously describes as only suggestive—indicates that damage to the blood–brain barrier may play an indispensable part in the pathogenesis. Such damage may not occur in animals receiving the drugs.

The importance of this experimental work has been increased by the inclusion in the group of diseases characterized by acute perivascular myelinoclasis[17] of the rare neurological complications of measles, influenza, smallpox, chicken-pox, German measles, and mumps. In addition there are similarities between acute haemorrhagic leuco-encephalitis[18] and some of the more acute lesions seen by Kabat and his colleagues[11] in monkeys. Application of the knowledge gained from these investigations to our understanding of demyelinating processes in man, and in particular the evolution of the larger and more chronic progress of disseminated sclerosis, must await further clearing of the experimental field.

TREATMENT OF PERFORATED ULCER

The "conservative" or non-operative treatment of acute perforated peptic ulcer is by now well known, though how many surgeons have the courage to rely on it is undetermined. That the number is considerable can be accepted from the several articles published in the last two or three years. These have recently been reviewed by Hermon Taylor,[1] himself an enthusiastic advocate of the method. In all, he reports on 555 cases from various countries. Undoubtedly it does demand courage to "wait and see" once the diagnosis of perforation has been made. For one thing, however convincing the physical signs may be, the diagnosis may be wrong and the ubiquitous appendix may be the cause of the board-like rigidity and all the other signs and symptoms. Admittedly the modern practice of taking a skiagram of the abdomen to show free gas makes this possibility more remote, but many surgeons have been caught out on occasions, and those who have do not easily forget.

The reasons which led the pioneers of the method to sheathe their knives hardly need repetition. As the late Hedley Visick wrote in 1946,[2] there was already a trend towards conservatism in that the "thorough peritoneal toilet" had been abandoned and drainage largely given up. It was widely recognized, too, that frequently the omental plug which had successfully sealed the perforation had actually to be removed before the leak could be found. Again, all surgeons had experience of the case that had been missed or of the patient who had recovered in spite of being too ill for laparotomy. Bedford-Turner[3] established the vital importance of keeping the patient quiet, the stomach empty, and the fluid balance properly adjusted. To these may now be added the benefits of antibiotics. It was in these circumstances that trials of the method have been considered practicable. One such trial is reported on page 1013.

Also in this issue we publish an article by Mr. A. Davis Beattie describing a carefully conducted investigation extending over three years and including 40 patients. This is a fair number, considering that the strictness of his criteria of perforation should satisfy any doubter. He calls his article the *expectant* treatment of perforated peptic ulcer, thus leaving what in current diplomatic parlance is called an escape clause. This meant that if a patient deteriorated operation was considered. The decision was usually taken between 24 and 48 hours after the beginning of treatment, but surgery was found necessary on only three occasions. Beattie believes that chest complications are worse without operation than following it. Perforated duodenal ulcers, he has observed, become sealed off better than gastric ulcers, and of the latter it is those on the anterior surface of the stomach which are the most lethal. It is because of this impossibility of being sure where the perforation is situated and how large it is that he ends his article with the words: "The expectant method of treatment has now been abandoned in favour of early laparotomy in every case."

The discussion on whether to operate or not naturally revolves around the question of mortality. It is accepted that under the best conditions laparotomy does not carry a mortality of more than 6% at most, and Beattie found that expectant treatment cannot better this figure. In 1946 we remarked in a leading article[4] that "the results of operative treatment . . . are so much better than those advanced by the advocates of conservatism that non-operative treatment should be reserved for the poor-risk cases only." But it seems that in view of Taylor's recent personal figures and those quoted by him from other sources, besides later reports,[5] this statement was too sweeping. The fatality rate among those treated conservatively compares very favourably with the rate among surgically treated patients. Those surgeons who have never had conservative sympathies, at least in this respect, will delight in Mr. Beattie's conclusion. But it must be observed that since 1945 the case for the opposition, to judge from published figures, appears to have become stronger.

1 *Lancet*, 1951, 1, 7.
2 *British Medical Journal*, 1946, 2, 941.
3 Ibid., 1945, 1, 457.
4 Ibid., 1946, 2, 948.
5 Scott, E., ibid., 1951, 1, 675.

TREATMENT AT SPAS

Some years ago at an Annual Meeting of the Association a distinguished physician, in opening a discussion on the treatment of chronic rheumatism, remarked that the value of treatment at spas had been recognized almost from the beginning of history and critically discussed the basis of this reputation as well as that of other forms of physiotherapy. While admitting the value of spa methods, he concluded that they might be made available without the necessity of visiting the spa. Though this may be true of the physical methods, such a view does not take note of the other features which play a part in the spa—the rest and holiday from domestic duties and from the strain of business, the benefits of a physical environment which usually, within geographical limits, is as good as man and nature can provide, and recreation for both mind and body. In many Continental spas diet is a conspicuous part of the cure, but this receives little scientific attention in most British spas. In the sixteenth century, when spa treatment was being sought by many sufferers, diet was not neglected, for Queen Elizabeth herself wrote these instructions (suggestive of modern rationing) to the Earl of Shrewsbury about the meals appropriate for certain of the courtiers who were under treatment while residing at his house in a certain spa:

"We think it meet for the saving of our credit to prescribe unto you a proportion of diet which in no case you shall exceed, that is to allow him [Lord Leicester] by the day of his meat two ounces of flesh, referring the quality to yourselves so as you do not exceed the quantity, and for drink one twentieth of a pint of wine to comfort his stomach and as much of St. Anne's sacred water as he lusteth to drink. On festival days, as is fit for a man of his quality, we can be content you shall enlarge his diet by allowing him for his dinner the shoulder of a wren and for his supper a leg of the same beside his ordinary ounces. The like proportion we mean you shall allow unto our brother of Warwick, saving that we think it meet in respect that his body is more replete than his brother's that the wren's leg allowed at supper be abated."

Because of advances in medical knowledge and changes brought about by the National Health Service, the British Medical Association decided that a concise scientific statement on the place of the spa in the field of medicine to-day should be prepared, primarily for the information of general practitioners. A committee of distinguished physicians, under the chairmanship of Lord Horder, was therefore appointed last year to survey the position, and its report,[1] which is summarized in this week's *Supplement*, deserves the careful attention of the profession. The fact is stated at the outset that the medical student receives little or no instruction in the special treatment given at the spas, and as a result many practitioners are unaware of the valuable work done there. Now that the spas are to be more widely used in the National Health Service, university research departments could perhaps give more attention to spa treatment, but the problem of providing controls in clinical research presents a difficulty. Professor Whitridge Davies and Dr. Geoffrey Holmes began some work of this nature at the University of Leeds in 1930, but they were unable to carry it very far, though J. B. Burt's observations on certain spa waters were of much interest and importance. Bearing in mind the need of the general practitioner for information about spas, the committee has included in the report chapters on the indications for and the techniques of spa treatment, in addition to a short description of the spas in England and Wales, each with a note about the conditions suitable for treatment. Provided the ordinary formalities are observed any patient may obtain out-patient treatment under the N.H.S. at any spa hospital, but at present patients living in hospital regions possessing no spa may have difficulty in gaining admission to a spa hospital. The committee rightly thinks that in-patient treatment should be related mainly to medical, and not only to geographical, considerations.

The committee's report refers to the long-continued arguments about the therapeutic specificity of different spa waters. Statistical evidence is lacking, but it is certainly not the experience of spa physicians that the same results will be obtained from a plain water as are claimed for mineral water. The difference in effect between the strong brine of Droitwich and tap water is obvious, and there are differences also in waters of low mineralization. To regard bathing merely as a way of applying heat is to ignore its action in raising resistance and toning up the peripheral circulation. Again there may be a tendency nowadays to ignore the effect of "taking the waters" internally, but a course of systemic water drinking, especially of the milder salines, can be of great benefit, especially to those who do not drink enough water or who drink too much of less suitable fluids. Too often the inclination of the patient rather than the prescription of the doctor determines the question, and the free elimination which is important in many forms of physiotherapy is neglected. The importance attached by the older physicians to the free action through the "primae viae" was exemplified by the prescription of suitable water in suitable quantity at suitable times in suitable cases, and sometimes this can still be a valuable part of spa treatment.

[1] *The Spa in Medical Practice*, 1951. Published by the British Medical Association, price 3s. 6d. net.

ENZYMES AND DIAGNOSIS

Enzymes are organic substances which catalyse the chemical reactions of living cells. Their measurement in body fluids as an aid to the diagnosis and treatment of disease is rapidly assuming more importance with the establishment of reliable and relatively simple methods of analysis. The phosphatases are probably estimated most frequently in clinical work; the value of serum alkaline phosphatase determinations in diseases of liver and bone is well known, as is the significance of a marked increase in serum acid phosphatase activity in malignant conditions of the prostate. Phosphatases have also been measured in other body

fluids; increased activity in cerebrospinal fluid has been reported in cases of meningitis and poliomyelitis,[1] and the change in the secretory activity of the prostate after psychic stimulation has been assessed by an increase in acid phosphatase activity in the urine.[2]

Acute pancreatitis has come to be regarded as a self-limiting disease, and significantly elevated values for serum and urinary diastase and serum lipase have been considered to be pathognomonic of this condition. It would therefore appear that the measurement of these enzymes in suspected cases of pancreatitis constitutes one of the most valuable biochemical aids in diagnosis. Recent work,[3] however, has shown that raised values for serum diastase and lipase may be found in cases of perforated gastric or duodenal ulcer, and elsewhere in this issue Dr. H. Wapshaw discusses the significance of these observations and the possible mechanisms involved.

Histaminase, which destroys histamine, is present in a number of tissues, but cannot be detected in the blood of men and non-pregnant women. During a normal pregnancy histaminase activity becomes apparent in the blood about the third month, increases to a maximum about the sixth month, and then decreases. Significantly low values have been reported in cases of threatened abortion and pre-eclamptic toxaemia.[4] A volumetric method of measuring histaminase activity is available, and this may prove a valuable aid in the investigation of the toxaemias of pregnancy.

Carbonic anhydrase, a zinc-containing enzyme present in erythrocytes, catalyses the hydration of carbon dioxide to carbonic acid, and also the reverse reaction. Altschule and Lewis[5] investigated a variety of blood dyscrasias and found that except in pernicious anaemia and myeloid leukaemia the anhydrase activity was proportional to the haematocrit reading. In pernicious anaemia the anhydrase activity per unit quantity of erythrocytes (i.e., the amount of enzyme in each red cell) was increased two to four times, returning to normal levels only late in treatment, and in cases of myeloid leukaemia an increase of 1.2 to four times the normal level was found. The zinc content of the erythrocytes has since been used as a convenient measure of the anhydrase activity.[6]

The hydrolysis of acetylcholine, liberated at the cholinergic nerve-endings, appears to be performed by at least two types of enzymes, a specific or "true" cholinesterase and a non-specific or pseudo-cholinesterase. In myasthenia gravis a disturbance of the balance between the rate of liberation of acetylcholine at the neuromuscular junction and the rate of its hydrolysis by the cholinesterases may be of great importance, but Wilson, Maw, and Geoghegan[7] found no significant differences between the true and pseudo-cholinesterase activity in blood and muscle in patients with myasthenia gravis and in normal subjects. The cholinesterase activity in blood has been used in the differential diagnosis of jaundice,[8] low values being obtained in cirrhosis and in malignant obstruction, whereas in infective hepatitis the values, though low at the peak of the disease, rose during convalescence.

The measurement of phosphatase activity remains the most useful routine enzyme estimation, especially since recent work on perforated ulcers casts doubt on the significance of elevated values of serum amylase and lipase in the diagnosis of acute pancreatitis. It is too early to assess the practical value of the determination of enzymes such as histaminase, carbonic anhydrase, and the cholinesterases. Further work is necessary before their status as diagnostic aids in clinical medicine can justify their routine estimation in body fluids.

1 Colling, K. G., and Rossiter, R. J., *Canad. J. Res. Sect. E.*, 1950, **28**, 56.
2 Clark, L. C., and Treichler, P., *Psychosom. Med.*, 1950, **12**, 261.
3 Wapshaw, H., *Lancet*, 1949, **2**, 414: Musgrove, J. E., *Proc. Mayo Clin.*, 1950, **25**, 8.
4 Kapeller-Adler, R., *Biochem. J.*, 1951, **48**, 99.
5 *Blood*, 1949, **4**, 442.
6 Vallee, B. L., Lewis, H. D., Altschule, M. D., and Gibson, J. G., *ibid.*, 1949, **4**, 467.
7 *Quart. J. Med.*, 1951, **20**, 13.
8 Alcalde, J. M. O., *J. Lab. clin. Med.*, 1950, **36**, 391.

SURVIVAL OF BACTERIA ON SWABS

The collection of pathological material on cotton-wool swabs has become a very widespread practice, despite the fact that better specimens can sometimes be obtained with a little care in a different way. First introduced for the diagnosis of diphtheria and other diseases of the nose and throat, it has been extended to inflammatory exudates generally in wounds and other lesions, and more recently even to the lower bowel—rectal swabs replacing faeces in the diagnosis of intestinal infections. It has always been recognized that certain bacteria, notably gonococci and meningococci, will not survive long under such conditions, and special methods have been devised to meet this difficulty. But if the examination of a swab has to be delayed, it is also advisable to confirm that the general run of rather hardier pathogenic bacteria will survive in adequate numbers under the conditions afforded by transit on a swab of any particular type. It is to this problem that Dr. S. D. Rubbo and Miss M. Benjamin, of Melbourne, have addressed themselves, and an account of their findings appears on page 983.

When swabs were dipped in a weak bacterial suspension in tap water and cultivated at intervals, it was found that on swabs made with certain brands of cotton-wool the bacteria died out quickly. This difficulty could not be overcome by choosing a suitable wool and using it exclusively, since the behaviour of a given manufacturer's product was not constant. It may be said here that this is a severe form of test, since it is well recognized that bacteria live longer in natural material containing plasma proteins or mucin than in water. It is mentioned later in the paper that other suspending fluids were tried, including saliva, with similar results: it must therefore be accepted that some cotton-wools contain an unknown bactericidal substance, and swabs made with them, if not cultivated within a short time, will give false negative results. The remedy proposed is to dip the swab in serum, sterilizing it subsequently by autoclaving. Such swabs, even if made with deleterious wools, were found to ensure prolonged survival. This was confirmed not only by artificial laboratory tests

but by using both serum and ordinary swabs in cases of haemolytic streptococcal throat infection. Delayed culture gave a substantially higher proportion of positives from the serum swabs.

These experiments also brought out other interesting points about particular classes of bacteria: these are mainly confirmatory of existing knowledge obtained in somewhat different ways. There is a sharp contrast between the behaviour of the pyogenic Gram-positive cocci and intestinal Gram-negative bacilli in relation to moisture. Drying in the presence of serum favours the survival of the former: this tallies with the known persistence of such organisms in the dust of septic wards. It may be added here that diphtheria bacilli will also survive for at least a month in dust, and it seems doubtful whether the authors' solicitous care for the welfare of this species is justified either by their own findings or by the known features of its behaviour. Intestinal pathogens, on the other hand, abhor drying, as their natural proclivities would lead one to expect, and it seems as if special moistening of swabs used for material which may contain them would be a useful precaution—if it be granted that a swab is the right sort of specimen for the purpose. It is interesting that deleterious wools have apparently no effect on this class of organism. The authors also investigated the effect on survival of other possible factors and indicate the survival times to be expected for different bacteria. The use of the "serum swab" should evidently commend itself to laboratories receiving specimens from a distance.

EYE MOVEMENTS

Whether or not the recording of eye movements will eventually be put to clinical purposes, recent work has demonstrated its physiological and psychological interest and has directed attention to the importance of eye movements in special activities such as flying. The need to direct the eyes from one point in the visual field to another arises from the high resolution associated with the fovea, the area of keenest vision, in the centre of which, according to Polyak,[1] there exists a bouquet of some 2,500 very narrow cones occupying a circular area about 0.1 mm. in diameter. The visual axis of the eye in fact behaves very much like a pointer which has to be directed on to the object under regard, but questions have been raised about the precision with which it is directed on to any particular point in space. Is there one cone of pre-eminent importance in the retina at the point where the visual axis of the eye, the line of sight, cuts it? Is there a fixation field rather than a fixation point? Does the eye remain absolutely steady during fixation? Can the extraocular muscles control the rotation of the eye to a precision of half a minute of arc or less as required if the visual axis were defined by a single cone, and can the two eyes be rotated in harness together to this precision?

Experiment has not given an unequivocal answer to these questions. Subjective tests, such as finding the smallest spacing between a row of dots that will still allow the dots to be counted, suggest a limit of some three or four minutes of arc to the precision of fixation. Objective methods are more difficult to interpret. They usually record the movements of the light reflected from the cornea, or, in some cases, from a contact lens fitted over the cornea, and the assumption has to be made that the centre of rotation of the eye occupies a fixed position in the eyeball and is more or less coincident with its anatomical centre. Neither of these assumptions may be strictly true, and they may be important subjects of investigation in themselves in relation to the development of visual fatigue, especially in ametropia. Moreover, even if the eyeball rotation were accurately known, the corresponding movements of the image across the retina can be deduced only on the assumption that the crystalline lens is immobile within the eyeball. This, too, has been questioned by some workers.

Nevertheless, recent reviews,[2,3] have reported very considerable activity in this field, in which photographic and photo-electric recordings of the corneal light reflection, and recording the corneal–retinal electrical potential difference, have all been employed with some success. Nearly all the results agree that during supposed steady fixation the eyeballs do undergo some movement, if only by small angles of a few minutes of arc, but that some people are steadier than others. Some records show a kind of nystagmic flick occasionally, which may be of biological significance in preventing prolonged local adaptation of the retina. One of the major experimental difficulties concerns the movement of the head; attempts are usually made to fix it as precisely as possible relative to the recording apparatus, but the artificial restraints which this involves may themselves disturb the subject and affect his eye movements. Nevertheless, there are successful records of both the smooth pursuit movements that occur when the eye follows a moving target and the saccadic (jerky) movements that appear to be a feature of most other conditions of observation.

Present experimental techniques appear somewhat complicated for direct application to clinical work, and it is to be hoped that simpler apparatus capable of recording the essential information can be developed. A study of the different types of nystagmus, and records of nystagmic movements in their early stages, would be of interest. Correlation of eye movements with neuromuscular disorders may also prove important, and an investigation should also be made to determine whether there is any relation between eye movements and visual fatigue. In connexion with the design of visual aids for landing an aircraft in bad visibility it has been considered worth while to make a film of the pilot's eye movements,[4] and it was found that there are relatively long periods when the pilot stares straight ahead. Analogous studies for other types of visual task, notably car driving, would appear to be justified.

1 *The Retina*, 1941. University Press, Chicago.
2 Carmichael, L., and Dearborn, W. F., *Reading and Visual Fatigue*, 1948, Harrap, London.
3 Lord, M. P., and Wright, W. D., *Rep. Prog. Physics* (Phys. Soc.), 1950, 13, 1.
4 Calvert, E. S., *Trans. ill. eng. Soc., Lond.*, 1950, 15, 183.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

MINOR AILMENTS OF THE FEET—I

BY

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Despite the great modern-day use of mechanical transport, or possibly because of it, minor ailments of the feet seem to be increasingly encountered in medical practice, so that the doctor is often asked to give advice upon and to treat such conditions. Unfortunately there are a large number of foot troubles, and I shall deal only with the commoner ones.

Corns

At the head of the list comes the ubiquitous corn. Most of these, however, are handled by the sufferers themselves or by chiropodists, and only the more persistent and troublesome ones will reach the doctor. Footwear is usually held to blame for the production of corns, but it must be remembered that without counter-pressure the shoe could do no harm. This counter-pressure is provided by structures in the foot, usually by bone. Thus deformed bones, enlarged joints, contracted toes, and so on are found underlying corns (with the exception of seed corns and the so-called vascular or neurovascular corns, which have a different aetiology) and share with the shoe in the production of the corns. Sometimes, however, one structure in the foot provides the counter-pressure for another, as in the case of soft corns lying in the fourth interdigital gap where pressure occurs between the head of the proximal phalanx of the fifth and the base of the proximal phalanx of the fourth toe.

The outer toes in the human foot are rather insignificant digits and the phalangeal shafts are disproportionately small as compared with the articular ends of the bones. This is a factor which concentrates the pressure and friction, between the toes or against the shoe, on small areas over the joints and so predisposes to corn formation at these points. In searching for the cause of recurrence of corns after treatment these are matters to which attention must be paid. Again some change of stance occurring automatically as a reaction to a painful lesion elsewhere in the foot or to an alteration in the balance higher in the limb may be responsible for the corn-producing pressure.

Unless and until such underlying factors can be remedied the corns will be prone to recur, the more so as skin which has once produced a corn seems predisposed to the production of others. The full investigation of a simple case of corns can thus involve the practitioner in a prolonged examination if the true cause is to be discovered. Disappointingly, when such causes have been found it is not always possible to remedy them by simple measures commensurate with the trivial, though troublesome, lesion they are producing. Thus excision of an enlarged toe-joint might relieve the pressure, but there are few who would be willing to submit to this. It will be easier in most cases to make the shoe fit the foot than the foot the shoe. This may be accomplished by having a special last made, or more simply, where the deformity is less marked, by having the shoe leather stretched over the critical point by carefully padded shoe-trees.

In practice treatment is often palliative—that is, the paring of the corn or callosity followed by protective padding. This is essentially work for the properly-trained chiropodist, but if the doctor undertakes it he must see that the central white dyskeratotic core of the corn is removed or there will be early recurrence. Alternatively the cornified epithelium may be softened and exfoliated by the application of a corn salve, the basis of which is salicylic acid, usually in collodion, and classically with a little cannabis indica. This method often gives relief but is not, of course, curative.

The commonest complications of corns are infection (Fig. 1) and suppuration. In many corns a small fluid-containing sac, often improperly called a bursa, forms in the deeper layers of the epidermis, and it is in this that infection arises either *de novo* or after treatment. As the overlying tissue is entirely epidermal, drainage is easily and painlessly instituted by skiving down the corn until the sac is reached. The corns which form over the prominence of a hammer-toe or clawed toe may, however, have a real bursa in the underlying dermis; here drainage will be painful without anaesthesia.

FIG. 1.—Hammer-toe with inflamed corn over the proximal interphalangeal joint.*

Callosities

The causative factors of corns and callosities are similar, but in the latter the pressures are distributed over larger areas of the surface either owing to the conformation of the bones or to the intervention of a thick pad of

*All the illustrations for this and the succeeding article on "Minor Ailments of the Feet" have kindly been provided by the Medical Photographic Department, Royal National Orthopaedic Hospital, London.

subcutaneous fibro-fatty tissue—for example, the callosities under the heel. Many callosities are harmless and some are beneficial, but when they occur in unusual situations—for example, under the heads of the second and third metatarsals—they are often troublesome and demand treatment. This must be directed not only to the reduction of the callosity itself but to the removal, if possible, of the causative factor, such as "dropping" of the metatarsal head. It may be interjected here that this is not a true dropping but implies that the particular metatarsal is carrying a greater proportion of the stresses of locomotion than it should normally do.

The second metatarsal is particularly prone to develop these painful thickenings under its head. There are several factors concerned in this, the most important being the relative projection forwards of the various metatarsal heads. Radiographs of the feet (in many cases this can be more simply determined by direct palpation of the bones) show that in about 50% of people the second metatarsal projects beyond the first, that in about 30% the first projects beyond the second, and that in the remainder the heads are level. When during walking the foot rises to the take-off position the metatarsals are almost vertical and obviously the one which projects furthest forwards will take most of the stresses. It should be noted that these figures are averages from normal feet.

If the great toe deviates away from the others—for example in splay-foot—or if its metatarsal is unstable, the stresses will fall on the second (and third) metatarsals whatever the relative lengths. These facts explain why the mere reduction of a callosity cannot bring about a permanent cure; a redistribution of the stresses is necessary so that the sturdy first metatarsal can again carry its proper large share of the burden. As it is usually not possible to change the anatomical conformation of the foot the desired effect must be accomplished by suitably fitted and shaped pads and elevators, the construction of which is beyond the scope of this article.

Forward Displacement of Pads under Metatarsal Heads

A condition in this region of the foot which has not yet received the recognition it merits is displacement forwards of the fibro-fatty pads which underlie the metatarsal heads and normally cushion the impact and pressure of these on the ground. The practitioner undoubtedly sees many of these cases; they occur chiefly in older people and particularly in women. The foot displays the characters which indicate that the patient has for long worn high heels—that is, it is plantar flexed, with a high rigid arch, clawed toes, callosities under the metatarsal heads, etc.—and the complaint is of pain on the plantar aspect of the anterior metatarsal region. "I feel as if I were walking on bare bones" is a common description. Upon examination it will be noted that the metatarsal heads are too readily felt in the sole. There is very little tissue between skin and bone, the normal pad having been displaced forwards as a roll of tissue under the proximal phalanges of the toes, which it has pushed up into the clawed position. This displacement occurs as a result of the forward rolling movement of the metatarsal heads, an action which is greatly enhanced when the heel is kept raised as in women's high-heeled shoes. The fatty pad is indeed being constantly heaped forwards like dough before a rolling-pin, and eventually comes to occupy the new position permanently; elevation of the proximal phalanx naturally follows.

The treatment of the condition is not easy, for the pads cannot be induced to retrace the movement by any simple measures. I have tried plastic surgical measures with mediocre success, but for the most part the condition must be accepted as a late outcome of high heels and a pad of sponge rubber or felt of suitable shape and thickness should be placed under the metatarsal heads. Any measure which relieves pressure on the bone heads—for example, metatarsal bars on or in the shoes—should be tried in these difficult cases.

Metatarsalgia

The term metatarsalgia is applied rather loosely to almost any pain in the anterior metatarsal region of the foot not due to some obvious external cause, but one well-defined type (distinguished by the eponym Morton's metatarsalgia) has been shown to have a precise pathological basis. This pain occurs predominantly in the region of the head of the fourth metatarsal and extends forwards to the digit, sometimes also to the third toe and rarely even further afield. It is an acute lancinating pain coming on, chiefly in women, after walking a short distance; it compels the patient to stop and not infrequently to take the shoe off and squeeze the foot. A change of shoe may give some relief, but on the whole the condition is progressive. The pain, at any rate in the early stages, disappears quickly with rest, but it may be

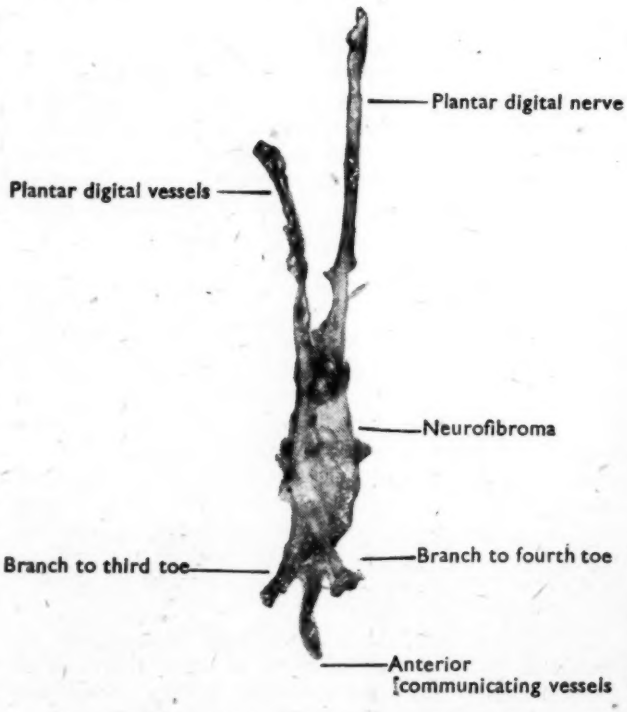


FIG. 2.—Morton's metatarsalgia: neurofibroma removed from the interspace between the third and fourth metatarsals.

associated with tingling and numbness of the toe. Morton ascribed it to nipping of the digital nerves between the metatarsal heads, but operative exposure has shown that a neurofibroma, the removal of which cures the symptoms, can usually be displayed on the communicating branch between the plantar nerves (see Fig. 2). In patients for whom surgical treatment is not available for one reason or another a good deal of relief is afforded by metatarsal bars or pads associated with a wide type of footwear.

Flat-foot

One of the commonest diagnoses made in the past to account for foot pain was "flat-foot." Nowadays we hear much less of this, for in many of the cases it is recognized that the disability is due to other causes occurring in a foot with a naturally low arch. The first thing to be said about flat-foot, therefore, is that most of the so-called cases are not flat-foot. Nevertheless there is a true condition of flat-foot (Fig. 3). There are two

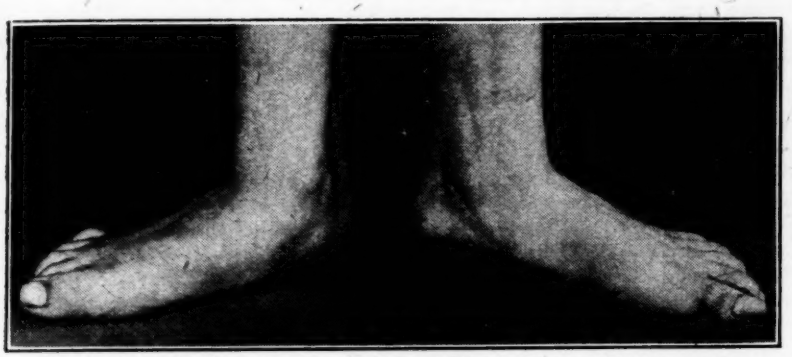


FIG. 3.—True flat-foot, showing the inner border in contact with the ground.

schools of thought regarding the formation and maintenance of the arches of the feet, but to consider the arguments for and against would occupy too much space. Briefly it must be stated that the arches of the feet vary within wide limits, so that the diagnosis of flat-foot should be made only in those cases which show definite changes in the arches. It is easy otherwise to be misled, for instance by intermittent claudication of the small muscles of the sole of the foot and of the calf, a pain which comes on like that of flat-foot after the patient has walked a short distance. In younger people the condition often designated "foot strain" may lead to misdiagnosis, as it is often associated with some degree of pronation of the forefoot.

When it has been concluded that the case is one of true flat-foot it is customary to divide the process into three stages. In the first the foot is normal in appearance when at rest, but the arch drops excessively on weight-bearing; in the second the arch is constantly dropped but can be returned on manipulation; in the third stage the arch is permanently down and cannot be restored except by forcible wrenching. In the last type there are usually well-marked arthritic changes present (rigid flat-foot.

Treatment in the first stage consists chiefly in exercises designed to strengthen the muscles, with perhaps the wearing of a light resilient support in the shoe, which is built up along its inner border. In the second stage the same treatment is applied but with rather more sturdy supports. In some cases it may be worth retaining the foot in an over-corrected position for a week or two at the start of treatment by means of a splint (split plaster would be suitable) which can be removed for massage and exercises. In the third stage it is sometimes best to leave the foot alone, since, though both foot and gait are ugly, the condition is often not very painful. In the painful cases gentle manipulation combined with treatment for the arthritis is advisable.

The use of supports is a controversial question which cannot be discussed here, but most flat-foot patients find them of value, even though they may be acting as splints rather than supports. Brief reference must be made to spasmodic and acute flat-foot. The former occurs in youths and is really a forcible eversion of the foot produced by spasm of the peroneal muscles (Fig. 4). The spasm is not infrequently associated with a toxic synovitis of one or more of the intertarsal joints, as can be demonstrated by the temporary cessation of spasm when the joint is injected with local analgesic. Septic foci elsewhere in the body have been held responsible, but in my experience they are rarely found. The treatment in severe cases consists in over-correction under anaesthesia followed by retention in a plaster case. Very intractable cases may actually need crushing of the nerve supply to the muscle.

Acute flat-foot arises after some particularly strenuous exertion, but may also appear more or less spontaneously in cases of gonorrhoea. In the former type rest and massage for a few days are all that is necessary; the latter type will very rarely be seen nowadays.

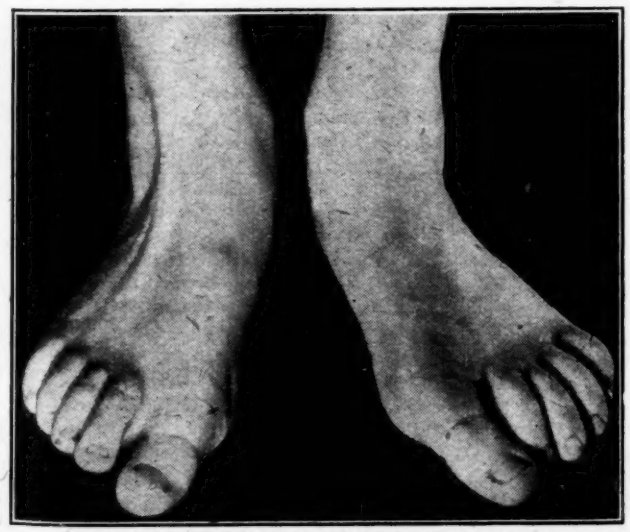


FIG. 4.—Spastic flat-foot. Note spasm of peronei.

The *Fifth Annual Report* of the Institute of Child Health, University of London, announces the proposal to build a model child-welfare centre and school treatment clinic on the corner of Lamb's Conduit Street and Guilford Street, near the Hospital for Sick Children. The architects are to be Messrs. Easton and Robertson, who are also to be responsible for the building of the British Postgraduate Medical Federation central offices (*British Medical Journal*, 1950, 2, 1400) on the adjoining corner of the north end of Lamb's Conduit Street, so that the two new buildings there can form part of a general plan. During 1950, 126 full-time students attended, coming from 21 different countries. Nine non-Commonwealth countries were represented during the year, showing that students from Europe are beginning to make London the centre for postgraduate study. Among other interesting research projects work on problems of blood disorders in the Postgraduate Medical School of London has been helped by members of the Institute, who have also served on the Joint Committee which (helped by a grant of £6,000 from the Nuffield Fund) has been following the health and development of a national sample of children. These children, born during the first week of March, 1946, have already been studied in 1946 and 1948, and information will be available for over 90% of the original sample of more than 5,000.

SOCIAL BACKGROUND OF INFANTS SUFFERING FROM DIARRHOEA AND VOMITING

BY

CONSTANCE A. C. ROSS, M.D.

(From the University and Knightswood Hospital, Glasgow)

The general statement is often made that social and environmental factors are of considerable importance in the aetiology of diarrhoea and vomiting of infancy. The high incidence of the syndrome in urban as compared with rural districts was shown by Gairdner (1944), who also gave figures indicating that illegitimate babies are much more susceptible to diarrhoeal conditions than those who are legitimate. Few attempts, however, have been made to investigate the influence of other social factors. The purpose of this report is to present some details of the domestic background of a group of infants admitted to the gastro-enteritis ward of this hospital during 1949.

Information was obtained by means of a questionary devised to assess housing conditions and "mother care." This questionary was completed by one of the child-welfare sisters, who visited the infant's home shortly after its admission to hospital. There was no selection of patients. The only criteria demanded were the pre-admission diagnosis of gastro-enteritis and that the child should be under 1 year of age.

Diarrhoea, either alone or accompanied by vomiting, is a common symptom of many disorders of infancy. These may be conveniently grouped in one of three broad categories—namely, dietetic diarrhoea, diarrhoea due to parenteral infection, and true gastro-enteritis. (In the last group no parenteral infection can be detected.) The cases in this series were placed in one of these three groups, according to the clinical history on admission and the clinical signs obtained within a week of admission.

Housing Conditions

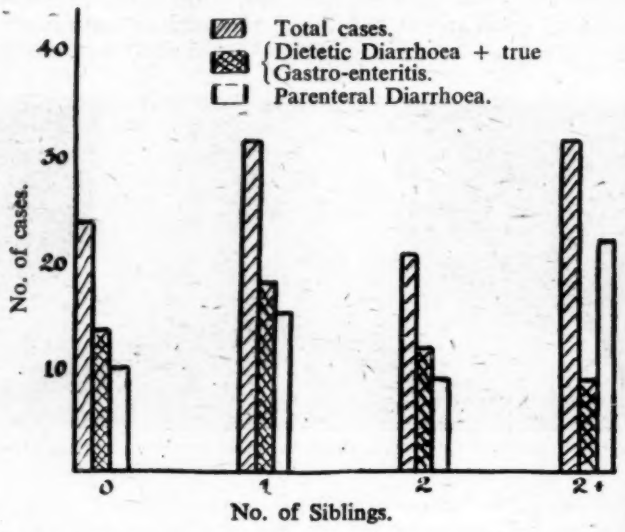
It will be seen from Table I that 61 (56%) of the 109 homes were "single ends." There was no hot-water system in 95 (87%) of the dwellings. An inside lavatory was present in only 34 (31%) of the homes, the remaining 75 (69%) sharing communal stairhead closets.

TABLE I.—*Housing Conditions of Enteritis Cases*

Type of Enteritis	Total Cases	No. of Habitable Rooms			Hot-water System		Inside W.C.		No. of Siblings			
		1	2	2+	Yes	No	Yes	No	0	1	2	2+
Dietetic diarrhoea ..	37	23	9	5	3	34	9	28	9	11	11	6
Parenteral diarrhoea	57	30	18	9	8	49	21	36	10	15	9	23
True gastro-enteritis ..	15	8	6	1	3	12	4	11	5	6	1	3
Total ..	109	61 (56)	33 (30)	15 (14)	14 (13)	95 (87)	34 (31)	75 (69)	24 (22)	32 (29)	21 (19)	32 (29)

Figures in parentheses represent percentages.

Subdivision of the cases according to size of family showed that 77 (70%) of the infants came from families of three children and under, and that 56 (51%) were either first or second children. No control figures are available for comparison, but this rather high proportion might suggest that the mothers' ignorance of infant feeding played an important part in initiating the syndrome. It is of interest to compare the family size of the two broad groups—those with dietetic diarrhoea and true gastro-enteritis (which may be considered together because as yet there is no absolute aetiological distinction between them)—and those secondary to a parenteral infection (see Chart). In the infants with three or more



siblings the commonest cause of enteritis was a parenteral infection. This would rather suggest the importance of overcrowding and the intrafamilial cross-infection to which it gave rise.

"Mother Care"

It is obviously more difficult to assess "mother care"; nevertheless it is considered that the extensive experience of the child-welfare sisters in home visitation gives a broad accuracy to the figures. They were able to estimate the intelligence, personal cleanliness, and housekeeping abilities of the mothers with far greater accuracy than could be achieved by any interview at hospital.

Table II shows that only 34 (31%) of the mothers attended a child-welfare clinic on two or more occasions. It is noteworthy, however, that only 26 (24%) of the mothers were regarded as of poor intelligence, and only 17 (16%) were untidy in appearance.

TABLE II.—*Assessment of Mothers*

Type of Enteritis	Total Cases	Attended C.W. Clinic		Appearance of Mother			Intelligence of Mother		
		Yes	No	Cared For	Intermediate	Unkempt	Good	Aver.	Poor
Dietetic diarrhoea ..	37	14	23	9	22	6	6	22	9
Parenteral diarrhoea ..	57	17	40	14	34	9	7	36	14
True gastro-enteritis ..	15	3	12	4	9	2	2	10	3
Total ..	109	34 (31)	75	27	65	17 (16)	15	68	26 (24)

Figures in parentheses represent percentages.

Discussion

The picture revealed by these figures is indeed depressing. In such a group the occurrence of enteritis is not surprising. Indeed, that these babies should survive at all seems almost incredible. Of the social factors studied

here, it would seem that poor housing conditions are intimately related to the occurrence of diarrhoea and vomiting of infancy.

Now, it might be argued that infants with enteritis from good homes are probably not admitted to hospital, and that any survey of hospital cases is therefore not representative. Most general practitioners, however, realize that the outcome of even a mild enteritis in infancy is unpredictable. Moreover, they recognize the value of hospital treatment in dehydrated infants. It is thus likely that the present survey depicts with fair accuracy the social background in Glasgow of cases of diarrhoea and vomiting of infancy.

The precise aetiological relationship of poor home conditions has yet to be determined. Infection probably plays some part in the aetiology. Under such conditions as have been described it is certain that feeding-bottles are not boiled regularly, that napkins are washed infrequently, and that even hand-washing before making up feeds becomes almost impracticable. It is interesting that no breast-fed babies were found in this series, and of course breast milk is less liable to bacterial contamination than artificial feeds. It may, however, be argued with some cogency that under such social circumstances nutritional factors may be of considerable importance. Many of these infants were underweight, and some marasmic. Inquiry often revealed gross dietetic mismanagement. Moreover, as breast milk is the perfectly balanced food for the young infant, the greater susceptibility of the artificially fed to diarrhoea and vomiting may well be nutritional in origin.

I wish to acknowledge with grateful thanks the work of Dr. N. I. Wattie, senior medical officer, Glasgow Maternity and Child Welfare Services, and the child-welfare sisters. Without their invaluable co-operation this investigation could not have been carried out.

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Nova et Vetera

NEW NOSES FOR OLD

The Life and Times of Gaspare Tagliacozzi, Surgeon of Bologna, 1545–1599. With a documentary study of the Scientific and Cultural Life of Bologna in the 16th Century. By Martha Teach Gnudi and Jerome Pierce Webster. Preface by Arturo Castiglioni. (Pp. 538; 77 plates. $15.) New York: Herbert Reichner.

This magnificent volume, printed in a limited edition in Italy but in the English language, commemorates the life and work of the most famous of all plastic surgeons, Gaspare Tagliacozzi. Miss Gnudi is already well known for her admirable translation from Italian of the first work on scientific metallurgy. Dr. Webster, who spent five years teaching surgery in China and did distinguished work in the first world war, is an eminent exponent of plastic surgery. Their book contains, among other things, a history of anatomical and surgical teaching in the University of Bologna, which is the oldest medical school in Europe attached to a university. The practice of public dissection began there in the fourteenth century, even earlier than at Padua, and it has been continuous ever since.

Plastic surgery did not start with Tagliacozzi. It was practised in ancient India in the pre-Christian centuries, and there are traces of it among the Greeks. It was taken up in the later Middle Ages in south Italy. Notably two of the name of Branca, in Sicily, brought the art to considerable perfection in the fifteenth century. It was oftenest practised on the nose. In an account by a Bishop of Lucera toward the end of the fifteenth century we read:

"Illustrious indeed through all these times is Branca, the Sicilian, outstanding among all the surgeons of the whole world. He invented in that art a certain thing worthy of admiration and indeed almost incredible. For he conceived a method by which he could restore and repair mutilated noses. His son Antonius added not a little to this fine discovery of his father. Indeed he discovered a method of repairing not only noses, but lips and ears."

This art was not confined to Italy, but was practised also in France and Germany. About the middle of the fifteenth century the military surgeon Heinrich von Pfolspeundt wrote:

"To make a new nose for one who lacks it entirely and the dogs have devoured it.—If a person comes to you, whose nose has been devoured, and you wish to make a new nose for him, make him promise you solemnly to conceal how you wish to heal him. And after the vow, tell him your opinion. If he wishes to risk it tell him how you must cut and also bind him and how long he must be in bed. And allow no one to watch, so that he may not learn the art from you. Then either you or he must find a trustworthy person who will also promise to conceal the matter, and whom you may allow to observe, provided he be of aid to you and also help the patient to eat and drink and bring him other necessary things. And the room wherein he lies must also be locked. Let no one have access except the person who is to serve you and him."

Plastic Operations

Tagliacozzi worked and wrote more than a hundred years after these men. He was well trained in surgery at Bologna by Aranzio (1530–89), an excellent anatomist, still remembered for his contributions to heart anatomy and himself a plastic surgeon. Tagliacozzi became the professor of surgery in 1586. From the first he was attracted to the plastic side of the art. In the year of his appointment he addressed a letter on it to Mercuriale, the famous writer on gymnastics. Tagliacozzi's crowning achievement is his great *De Curtorum Chirurgia* ("On the surgery of deformities") (1597). This contains a series of figures illustrating plastic operations, the best known being that of a patient whose left arm is bound to his head while a flap of skin from over the biceps has been attached to his mutilated nose. The poor wretch had to remain in this position for some weeks, when the flap, having obtained new vascular connexions, was severed from the arm and more neatly tucked in round the nostrils.

This operation has been commemorated in several literary works. The most entertaining version, which should still add to the gaiety of nations, is a perverted account of the original. It is a translation by Walter Charlton (1619–1707), a medical gas-bag of the Restoration, whose language is as fantastic as his ideas. He took it, in turn, from a treatise by Van Helmont, of Brussels (1577–1644), on the "sympathetic" treatment of wounds:

"This one experiment, of all others, cannot but be free from all suspect of imposture, and illusion of the Divil. A certain inhabitant of *Bruxels*, in a combat had his nose mowed off, addressed himself to *Tagliacozzus* a famous Chirurgeon, living at *Bononia*, that he might procure a new one; and when he feared the incision of his own arm, he hired a Porter to admit it, out of whose arm, having first given the reward agreed upon, at length he dig'd a new nose. About thirteen moneths after his return to his own Countrey, on a sudden the ingrafted nose grew cold, putrified, and within a few days, dropt off. To those of his friends, that were curious in the exploration of the cause of this unexpected misfortune, it was discovered, that the Porter expired, neer about the same punctilio of time, wherein the nose grew frigid and cadaverous. There are at Bruxels, yet surviving, some of good repute, that were eyewitnesses of these occurrences. Is not this Magnetism of manifest affinity with mummy, whereby the nose, enjoying, by title and right of inoculation, a community of life, sense and vegetation, for so many moneths, on a sudden mortified on the other side of the Alpes? I pray, what is

there in this of Superstition? What of attent and exalted Imagination?"

What indeed?

Tagliacozzi was certainly one of the most eminent and successful surgeons of his century. We have here at last a worthy memorial of his work, combined with a history of plastic surgery. The book is extremely well illustrated, and ends with 22 full-page facsimiles of the plates in the volume of Tagliacozzi himself. The volume is in all ways a credit to authors, printer, and publisher. It is further adorned with a preface by the veteran medical scholar, Professor Arturo Castiglioni.

CHARLES SINGER.

Reports of Societies

LABORATORY FACILITIES IN GENERAL PRACTICE

To get his patients *x*-rayed and "pathologized" promptly, efficiently, and without recourse to a middleman (if hospital consultants will excuse the term) is a standing problem for every general practitioner who wants to hold up his head among his colleagues and to give his patients the service they ought to expect from him. Dr. J. H. HUNT, addressing the General Practice Section of the Royal Society of Medicine on April 18, gave this important subject an airing and showed how he has solved it for himself and his patients. After five years of war service Dr. Hunt returned to practice in S.W.1 to find, packed in a trunk by mistake at the outbreak of war, a specimen of urine still awaiting examination. He found also a legacy of pathological equipment from a friend "in practice round the corner" who had been killed at Dieppe.

Necessity is the Mother of Invention

Thus stung and persuaded into action, he equipped a laboratory in a tile-lined empty kitchen under his consulting-room and secured a skilled and experienced pathological technician to work there. He secured also the help, as consultant and overseer of his clinical pathology, of the pathologist of his own teaching hospital.

Later, kind chance disclosed a mews cottage behind his room in which to house his *x*-ray unit. He acted promptly, obtained most appropriate assistance, and was soon equipped with "an *x*-ray tube, a developing-room, and a first-rate, full-time radiographer." Turning again to his mother hospital he found a radiologist ready to see and report on every film taken. "He visits us once or more a week, when we go through the films together with the clinical notes beside us."

This team, strengthened later by an assistant practitioner, has been working now for five years, and Dr. Hunt, after describing in some detail his whole diagnostic and record-keeping equipment, went on to summarize the work done and assess its value to his patients and to himself as a perpetual student.

In the five years there have passed through his hands more than 3,800 patients, for whom over 7,000 pathological and 1,476 *x*-ray investigations have been carried out and 118 electrocardiograms taken. Dr. Hunt showed tables analysing the tests performed, the regions *x*-rayed, and the diseases and disorders in whose diagnosis and treatment the investigations played a part. He expected criticism from radiologists and pathologists, but was prepared to receive and profit by it if it came, and also prepared to justify the number of investigations made and to make good their claim to be useful and necessary. He put in a strong plea for the provision by the State of these necessary diagnostic aids for the direct use of all practitioners, inside the N.H.S. or out. "The important thing is for the family doctor to be able to ask for them himself and to have them done somewhere near him." He was by no means suggesting that his own "set up" should or could profitably be repeated in detail elsewhere; it did no more than exemplify the need and show a solution possible in certain circumstances.

If Dr. Hunt looked forward to contending with critics he was disappointed. Later speakers were at one in praising his initiative and enterprise and approving the work done.

Right of Direct Access to a Laboratory Report

Dr. R. BODLEY SCOTT mentioned the feeling that it was not quite cricket to solve clinical problems with the aid of the laboratory. This feeling perhaps underlay the barrier erected between the general practitioner and the laboratory. It was, he thought, almost the rule for the general practitioner to have to refer his N.H.S. patients to a physician when he required a blood count or a skiagram of the chest. That the necessary *ancillae* should be at the service of the man called upon to identify disease in its early stages was a self-evident principle, officially recognized indeed, but so far accorded little but lip service. A reported project of the Nuffield Trust gave him some hope that regional authorities might develop further units of this kind.

Mr. J. B. HEDLEY ATKINS, "brought up as a child by a general-practitioner father," found, to his distress, that all was not well with his brethren. They felt frustrated. One after one their sources of interest were taken from them until they wondered "whether in the end they would act as little more than sorting-houses in the vast, nationalized, impersonal, inhuman, incomprehensible, impoverished, irrational, fantastic, and altogether intolerable machine for the registration, documentation, statistical analysis, and occasional treatment of disease." Something of the sort was happening also in surgery. Not long since the knee-joint, the bladder, and even the inside of the skull had been within his province. Now he was just a general surgeon, "which simply means that the things we generally see generally belong to someone else."

The Germ of the Health Centre?

None the less the orientation of Medicine must change with advancing science; the best clinicians were those who completed their clinical examination with laboratory investigation. If general practice was to hold its field it must have something like the facilities for laboratory work created and described by Dr. Hunt. If the practitioner himself directed the work he would neither over- nor underestimate the value of the tests, but would be purposeful and economical in his demands. Patients would benefit by the speed and accuracy with which their diagnoses would be made.

If health centres must wait, laboratories might be created at less cost and might form the germ from which the health centres could grow in more propitious times. A levy on the corset like that to be imposed on the false teeth and spectacles might provide some of the sinews of war.

In the discussion that followed, Dr. GEOFFREY EVANS and Dr. J. D. SIMPSON emphasized the value of technicians, especially those from the Services. Dr. Simpson praised the married nurse as consulting-room assistant. From Kent, from Essex, and from the young city of Cambridge came cheering evidence that practitioners there had free access to hospital laboratories and could get at least most of the investigations they wanted done for them on demand. One of the witnesses, Dr. TALBOT ROGERS, pointed out that where such arrangements existed hospitals were not, in fact, swamped by needless demands, the general practitioner, in this respect, comparing favourably with the registrar. Hospital pathologists and radiologists, in his experience, welcomed this extramural work, finding that the practitioner was more apt than their hospital colleagues to treat them as consultants, not as mere purveyors of reports.

Dr. HUNT, replying, was glad to hear of the satisfactory arrangements in some districts, but was sure they did not exist everywhere.

PERFORATED PEPTIC ULCER

At a meeting of the Section of Surgery of the Manchester Medical Society, on March 13, a symposium on "The Treatment of Perforated Peptic Ulcer" was held.

Mr. T. HESLOP, in introducing the subject, said that, while the conservative treatment of perforated peptic ulcer had undoubtedly a place, the main difficulty was to formulate guiding principles on which to base a judgment in the individual case. Most of the previously published series had been selected cases, and, while these series had no doubt produced useful information, there was need for the comparison of parallel series of unselected cases.

For the past four years two parallel series had been treated at two adjacent hospitals in Salford. All the cases seen at Salford Royal were treated operatively, the few cases which had been treated conservatively there having been done in the early days of the trial. All cases admitted to Hope Hospital had been treated conservatively under the supervision of Mr. A. S. Bullough.

Results in the Series Treated by Operation

At Salford Royal Hospital Mr. Heslop and Mr. C. Brun had observed during the five-year period 1946–50 124 cases of perforated peptic ulcer. The total mortality had been 11—i.e., 8.8%, irrespective of the method of treatment. Of the 104 cases treated by emergency operation, nine died (8.6% mortality). Twenty unselected cases had been treated conservatively, and the mortality in this small group had been 10%. In this group subphrenic abcess had occurred once but had resolved after drainage.

The peak age incidence had been 30–39 years, and the sex ratio had been one female to 20 males.

The salient points about operative treatment were: adequate pre-operative preparation; the minimum of interference inside the abdomen—simple closure of the perforation and no exploration of the peritoneum; maintenance of gastric suction and controlled intravenous fluid administration for 24–48 hours; prophylactic chemotherapy; and early ambulation in the absence of complications.

The mortality depended on the time interval between onset and operation, the age of the patient (mortality increasing very much over 60 years), and the situation of the ulcer—perforated gastric ulcer (17 cases) carried a mortality of 30%, perforated duodenal ulcer (85 cases) only 5%. Of the nine fatal cases five only had died from general peritonitis within four days of operation.

The preponderance of peritonitis as a cause of death had been striking. When established on admission it was questionable whether operation was of any benefit, but when it developed after operation on early cases it could be traced to faulty operative technique or inadequate post-operative management, and these deaths should certainly be preventable.

Results in the Series Treated Conservatively

Mr. A. S. BULLOUGH reported his results with the conservative treatment of 102 consecutive cases of perforated peptic ulcer admitted since March, 1947, to Hope Hospital, Salford. His reasons for adopting conservative treatment were the high mortality of operated cases; the occasional recovery of unoperated desperate cases; the increasingly conservative operative measures; the fact that perforations were often found to be shut off at operation; the sterility of the fluid escaping into the peritoneal cavity. Treatment had consisted in the use of continuous gastric suction for several days, intravenous fluid therapy, and antibiotics. Patients had been more comfortable than those operated on, and were up and about and on light gastric diet within a week.

In the total series there had been eight deaths. Four were in elderly persons admitted moribund, long perforated, and quite unfit for any operation, who had died during the night following admission. They would not have figured in the mortality statistics of any operative series. The remaining four were late deaths (17 days to 8 weeks), and in all these there had been unsealed perforations with fistulae between stomach (two cases) or duodenum (two cases) and a cavity in the peritoneum containing gastric juice—not pus. In three the cavities had been drained, but they had developed external fistulae.

There had been 93 duodenal perforations with three deaths, and nine gastric perforations with five deaths. Of the four females in the 102 cases, one had died. There had been three true subphrenic abscesses with recovery in each case after drainage.

A possible criticism of the series was that it was impossible to be sure that all the cases had in fact perforated, although clinical experience, the subsequent course, radiographic evidence, and in some cases operation, had all tended to support the diagnosis. There was the risk of leaving unoperated some condition requiring operation: one such case had occurred. On the other hand, such conservative methods of treatment might conceivably preserve the lives of sufferers from coronary thrombosis, pneumonia, and acute pancreatitis by avoiding a dangerous operation.

CONGENITAL DISLOCATION OF THE HIP

At a meeting of the Section of Orthopaedics of the Royal Society of Medicine, held on April 3, a symposium on congenital dislocation of the hip was presented by Mr. J. S. Batchelor, Mr. H. J. Seddon, and Mr. David Trevor.

The treatment of congenital dislocation has been a matter of discussion and controversy almost since orthopaedics began. From the beginning of the century, closed manipulative reduction, as introduced by Lorenz, has been practised. A period of experimentation with the new technique was followed by a prolonged phase when a less traumatic closed manipulation than that described by Lorenz became generally accepted and practised. It is only in recent years that dissatisfaction with this method has been common and new methods have been developed. This long static phase is explicable when it is recalled that the end result is not known until the late decades of the patient's life.

Closed Reduction

It is now known that only about half the patients with congenital dislocation of the hip have a satisfactory result from closed manipulation. The hips of the remainder are either never reduced or redislocate, or they are attacked by a degenerative arthritis in early, middle, or late adult life.

Gentle closed manipulation is accepted as being the safest, easiest, and the most successful method of treatment. It is only in the "hard core" of cases in which closed manipulation has failed or is known to be impossible that open reduction becomes necessary. There is general agreement also that the younger the child the easier and simpler is treatment. The early diagnosis of the dislocated hip, suggested by a short leg or by difference in the levels of the gluteal creases on the two sides as well as by the better-known classical signs, still offers the easiest method of improving our results.

Mr. J. S. BATCHELOR surveyed the present position of closed reduction by reviewing the treatment of 40 children who had had 55 dislocated hips. Of the 55 hips primary reduction was not obtained in 7. Of the remaining 48, 14 redislocated after the removal of splintage. Ten of these redislocations were successfully treated, and stable reductions were eventually obtained in 44 hips (80%). The method of reduction consisted, first, in preliminary stretching of the contracted soft tissues by gradual abduction of both legs on a frame. When full (90°) abduction of both legs had been obtained, the child was removed from the frame and reduction attempted by internal rotation of the hip. The position of the hip was checked by radiological examination, and, if reduction was satisfactory, the legs

were splinted in a position of 90° internal rotation and 30°–40° abduction with knee plasters with a connecting bar. Avascular necrosis occurred in 18 cases, chiefly in hips which were reduced by manipulation under anaesthesia without preliminary correction of soft-tissue contracture.

Open Reduction

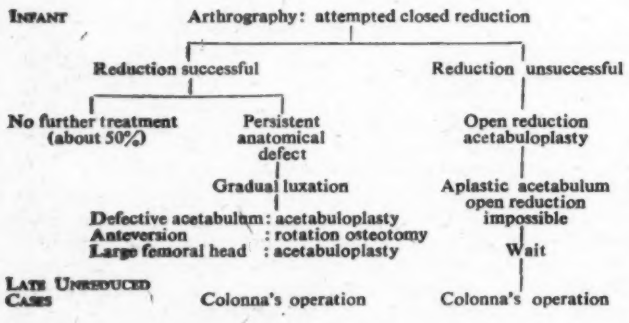
Mr. H. J. SEDDON reviewed a series of cases treated at the Royal National Orthopaedic Hospital. Closed reduction was always attempted first, by traction on a frame for not more than a month. Failure to reduce or subsequent redislocation was an indication for open reduction.

In the past the results of open reduction had been poor, one of the more important reasons being that few cases were operated upon until after numerous attempts at closed reduction; this had caused irreparable damage to the articular cartilage. Improved technique with anatomically sound operative approaches and blood transfusion had made open procedures less destructive and safer.

Arthrograms were used in all cases, frequently allowing one to predict whether open or closed reduction would be necessary; they also gave an idea of what operative procedure would be required on the soft tissues. In 27 cases in which open reduction had been performed the following soft-tissue obstructions to closed reduction had been observed:

High attachment of the inferior capsule	10
Hour-glass constriction of capsular neck	8
Infolded limbus	5
Excessive soft tissue in the acetabular floor ..	3
Enlarged ligamentum teres	1

While surgical correction of the soft-tissue obstruction allowed of reduction, bony abnormalities might render the latter insecure. If the acetabular roof were ill-developed or the femoral head relatively large the acetabulum required enlarging by a shelf operation (acetabuloplasty). Anteversion of the femoral neck was the other major bony abnormality that might cause redislocation; when present in an unusual degree it required correction by rotation osteotomy. This outline may be represented by the following diagrammatic scheme devised by Mr. Seddon:



Mr. DAVID TREVOR then outlined the operative procedure as performed by Mr. Seddon and himself. Although most of the open reductions had been done on older children, this had often been due in the past to unavoidable delay; open reduction had been done recently at approximately one year of age. The hip-joint was approached by a modified Smith-Petersen incision, the capsule-covered femoral head and acetabulum defined, and the obstruction to reduction removed. The operative findings were usually those expected from the pre-operative arthrogram. When the presence of a shallow acetabulum, especially if accompanied by a false acetabulum or a large femoral head, indicated that reduction would be unsuccessful, a low shelf (acetabuloplasty) was made by means of an osteotomy cut approximately ½ in. (1.26 cm.) above the true acetabular roof; this was then levered down and out so as to extend well forwards and backwards, and was fixed in position by an iliac graft.

A further indication for a shelf was a hip which had been reduced by the closed method and later developed a positive Trendelenburg sign; if left alone the hip would redislocate due to a shelving acetabulum. Another cause of redislocation was excessive, uncorrected anteversion. Rotation osteotomy was necessary to correct this and was better performed at a second operation, provided the acetabulum was adequate. The bone section was a high subtrochanteric one, and the fragments were held in the correct position by a small plate. For the late, unreduced hip Mr. Trevor advocated Hey Groves's operation as modified by Colonna.

In the ensuing discussion Mr. P. WILES stressed that many years would be required to assess the results of the procedures advocated. Mr. DENIS BROWNE disagreed with much that had been said, and advocated a closed reduction by posterior pressure on the trochanter. This was followed by a month in plaster and nine months' activity in the splint devised by himself. This splint held the legs abducted but allowed active weight-bearing and movement in one plane, thus achieving a secondary reduction through weight-bearing. He claimed that about 19 out of 20 cases could be successfully treated in this way.

ORTHOPAEDIC MISCELLANY

The Spring Meeting of the British Orthopaedic Association was held in Cambridge on April 6 and 7, 1951, under the presidency of Mr. S. L. HIGGS. Scientific papers were presented, and on the afternoon of the first day of the meeting a wide variety of clinical cases was shown at Addenbrooke's Hospital. One day was devoted to a symposium on "Congenital Dislocation of the Hip," at which Mr. H. J. SEDDON, Mr. DAVID TREVOR, and Professor R. MERLE D'AUBIGNÉ (from Paris) presented their results. Below are reported some of the other subjects discussed at the meeting.

Late Results of Lumbar Disk Operations

Of special interest to general practitioners was the discussion on the late results of lumbar disk operations. Mr. A. L. EYRE-BROOK gave an account of his results in 117 patients observed for one to six years after operation for sciatica, diagnosed as having been due to a disk lesion. He had studied in particular the future progress of patients in whom no causative pathology had been found on operation. Unless there was a definite protrusion or indisputable adhesions he regarded the exploration as negative; he did not believe in "hidden" disks or disk scars. In 117 operations the findings were negative in eleven; adhesions had been observed in six; and in the remainder a definite protrusion had been present. Results showed that 86% of patients in whom a definite lesion had been found had no more than very minor residual complaints after operation; of the 21 men with disk lesions who were engaged in heavy work before operation 18 were able to return to normal work. On the other hand, all except one of the patients in whom no lesion had been found had significant residual disability at the time of examination; in the one exception there was complete freedom from symptoms. Of the six patients in whom nerve-root adhesions had been found four had moderate relief and two had only slight relief.

Mr. JOHN CHARNLEY considered that lesions of the intervertebral disk fell into the province of the orthopaedic surgeon rather than the neurosurgeon. Exploration had been negative in 16% of his patients. In the earlier cases of his series he had sometimes failed to find lesions even when the straight-leg-raising test had been markedly positive; he considered that in such cases he had probably missed a disk protrusion at a different level. As his experience of the operation increased he found that negative explorations were less frequent and were usually in patients with only slight restriction of straight leg raising. He considered that the straight-leg-raising test was of the greatest value in diagnosis and assessment of the case for operation.

Mr. EYRE-BROOK, replying to the discussion, considered that, whereas lumbar puncture and myelography should be undertaken in problem cases, special investigations other than plain radiography were unnecessary in the straightforward case. Exploration of a disk was almost devoid of risk, and in the exceptional case in which the symptoms were found to be due to a tumour no great harm was done by the exploration. He did not consider that spinal fusion should be undertaken at the time of a disk exploration. If significant back pain arose afterwards it should be assessed as a separate problem in the same way as back pain from other causes. He agreed with Mr. Charnley that the straight-leg-raising test was the most significant sign.

Traumatic Aneurysm after Meniscectomy

Mr. T. J. FAIRBANK and Mr. E. S. JAMIESON described two cases of false aneurysm of the inferior lateral geniculate artery after lateral meniscectomy. The clinical features in the two cases were very similar. In each, a discoid cartilage had been removed. Tense haemarthrosis developed 11–12 days after operation and recurred after repeated aspiration. Six weeks after operation a pulsating swelling appeared over the lateral joint line in front of the lateral ligament, and a bruit was audible on auscultation. An arteriogram showed abrupt termination of the inferior lateral geniculate artery. In each patient the joint was explored and an aneurysm was found between the capsular and synovial layers. The damaged vessel was ligated, and ultimately good function had been regained though convalescence was slow. Anatomical studies had shown that the inferior lateral geniculate artery was liable to injury during lateral meniscectomy, especially if the plane of dissection wandered away from the synovium-cartilage junction. Injury seemed especially likely to occur during removal of a cystic or discoid cartilage. The vessel was probably injured more often than was realized, but if it was divided completely healing occurred through the usual process of retraction and coagulation. It was a wound of the wall of the artery without complete division that might lead to the formation of an aneurysm. It was suggested that if recurrent haemarthrosis arose after lateral meniscectomy it was advisable to explore the inferior lateral geniculate artery without delay. Mr. O. VAUGHAN-JACKSON mentioned a similar experience after medial meniscectomy in which the inferior medial geniculate artery was damaged. Mr. H. OSMOND-CLARKE had knowledge of a case in which a popliteal aneurysm arose after medial meniscectomy during which the surgeon had lacerated the capsule posteriorly and damaged the popliteal artery. The leg had had to be amputated. The case illustrated the necessity for great care in dissecting out the posterior part of a meniscus.

Pes Cavus

Mr. D. J. MARTIN discussed the aetiology and treatment of pes cavus. He believed that the essential defect was a lack of balance between the flexors and extensors of the foot, with relative weakness of the extensors leading to depression of the forefoot. The intrinsic muscles were not at fault, and shortening of the tendo Achillis was not a responsible factor. Clawing of the toes was secondary to the cavus deformity. Of the many operations that had been advocated for the treatment of disabling pes cavus he preferred a combination of Steindler's soft-tissue stripping in the sole with transplantation of all the long toe extensors into the metatarsal necks. This combined operation had been described by Todd, and in the speaker's experience it had given very satisfactory results. Mr. A. ROCYN JONES thought that Mr. Martin's assessment of the aetiology was correct, and he agreed that the operation described combined the virtues of the Steindler operation with those of transplantation of the extensor tendons. Mr. A. TODD was convinced that relative weakening of the extensors was in fact the primary factor in pes cavus, and that clawing of the toes was a secondary phenomenon; the Lambrinudi operation of multiple digital arthrodeses was accordingly unsound.

Correspondence

Calling all Athletes

SIR,—At the request of the Amateur Athletic Association, a small committee has been formed to advise and assist athletes in their various problems and difficulties, such as the details comprised under "training," the promotion and maintenance of fitness, the treatment of injuries incidental to sport, and so on. Such assistance, which has for long been available in the United States and on the Continent, has in this country been contributed only in a comparatively haphazard fashion by a few interested individuals. Now for the first time a systematic approach is contemplated.

It is clear that widespread co-operation of the profession is essential, and I shall be grateful for your generous allowance of space in order to appeal to colleagues throughout the British Isles and so to secure the technical knowledge and professional experience of a considerable number who in their youth were famous athletes. Their assistance is desired to give occasional advice to athletes in their neighbourhood, and, when convenient, to attend athletic contests. In this way no great demands will be made on their time, and they will have the satisfaction of performing a national service and of preserving their contact with athletics under the most advantageous circumstances.

Anyone interested is invited to communicate with Dr. John Etheridge, 73, Fitzjohn's Avenue, London, N.W.3, who will in due course forward further information.—I am, etc.,

London, W.1. ADOLPHE ABRAHAMS.

Breast-feeding

SIR,—As an upholder of breast-feeding for medical and psychological reasons, it is only since having children of my own that I have been able to appreciate in my work at the infant welfare clinics and in general practice the social causes which so often make the establishment of the natural function of breast-feeding an uphill task for both doctor and patient.

All-important, I think, is the attitude of the mother. An environment and upbringing which engenders a distaste for breast-feeding and favours a return to social life is found in all sections of society. Husbands often encourage this attitude, finding no beauty in the mother–child relationship—in fact, some may find it frankly disturbing. Many women start breast-feeding half-heartedly, possibly from a sense of duty, intending to fly to the bottle at the slightest pretext. Women are profoundly influenced by the many excellent advertisements for patent baby foods; on the other hand there is no similar publicity for the breast-fed baby.

Another important factor is the lack of domestic help. To most mothers the 10th day of the puerperium means a return to the usual household routine, plus the extra work and excitement of a new baby, without even a rest in the afternoon. This background—anything but tranquil—is enough to account for the shortage of milk and lack of confidence so common during the second and third weeks.

The interesting ethical question raised by Dr. J. D. Bottomley (April 21, p. 882) of giving stilboestrol tablets to a mother who asks for them depends, I think, on whether a doctor believes the mother should adapt herself as soon as possible to the present industrial society. The ethical problem is concerned not so much with the mother who asks for the tablets as with the society of which she is so typical a member. In this mechanical age people will use any machine or gadget rather than the human body.—I am, etc.,

Stoke-on-Trent. RUTH V. ROBSON.

SIR,—Dr. J. D. Bottomley's letter (April 21, p. 882) I find easy to answer. The mother who wants to suppress her milk for trivial and selfish reasons and does not yield to persuasion *must not* be given stilboestrol for the purpose, because it

relieves her of part of her responsibility. It is true that she will wean her baby in any case. It is also true otherwise, however, that she will report to a large circle of acquaintances: "The doctor gave me some tablets to take my milk away." She will be careful not to report that he did so under protest; and the incident will be interpreted as showing the doctor's approval of her reasons. Such incidents are, therefore, not self-contained. The principle to follow is, I believe: No interference without medical or economic grounds. (And one must be careful not to let "social" be substituted for "economic.")

Dr. Jean Lawrie's letter in the same issue (April 21, p. 882) is very interesting and important. I know of an area where the antenatal preparation for breast-feeding has been undertaken by the health visitors with great determination combined with tact, and they have achieved considerable success. However, it is clear from their case-records (which I have been allowed to see) that they cannot get any further because at present they have not got the co-operation of the local practitioners. When the mother has to call the doctor, he too often combines with his instructions about treatment a recommendation to put the baby on a bottle. The mother does not distinguish this from the rest of his instructions, and dutifully carries it out. One cannot in any way blame her for doing so. The fact remains that all the careful preparation and attentive supervision of the health visitor then goes for nothing because an ill-informed and thoughtless doctor has recommended bottle-feeding—without, probably, having the least idea himself why he did so.

I draw the conclusion that health visitors cannot do this work alone, and therefore one must still give first place to the conversion of the general practitioner—at least in his general outlook on the question. On the other hand there is no reason why the practitioner should himself give all the supervision that is needed unless he is alone in his area in thinking it necessary. In any area where there is agreement as to aims, there is everything to be said in favour of the doctors and the health visitors immediately joining forces—brought together by the medical officers of health, who can provide us with so many invaluable ancillary services.—I am, etc.,

York. F. CHARLOTTE NAISH.

Blood Pressure of Schoolboys

SIR,—Since my preliminary report on blood-pressure reading in schoolboys to which you kindly referred in your annotation (April 7, p. 750) was originally published in Dr. E. K. Macdonald's annual school medical officer's report (1949) I have extended the volume of the survey to more than 1,400 boys. The results of the findings and a statistical analysis of the correlation between systolic blood pressure and growth at this age period will, I hope, soon be submitted for publication. Although the values of the average systolic blood pressure, as you rightly expected, had to be corrected for the younger ages, the general trend remained unchanged.

The following table shows the mean ± statistical error of systolic and diastolic blood pressure for boys 11.5 to 15.5 years of age as found in the whole series.

Central Age: / Number:	11·5 / 211	12·5 / 126	13·5 / 118	14·5 / 880	15·5 / 83
Mean systolic B.P. ..	109·7	109·1	113·5	118·0	119·9
Stat. error ..	±0·78	±1·09	±1·3	±0·44	±1·7
Mean diastolic B.P...	62·5	63·3	62·1	66·7	68·2
Stat. error ..	±0·52	±0·77	±0·74	±0·30	±0·93

It can be seen that, whereas the difference between the mean values of the systolic blood pressure in the 11.5- and 12.5-year-old boys is statistically insignificant, there is a rise at 13.5 years—the time when in this country puberty starts. The increase is about the same between 13.5 and 14.5 years and slows down at the age of 15.5, thus approaching the average annual increase of 1 mm. Hg in the adults.—I am, etc.,

Leicester. LEO HAHN.

Syringe Needles and Mass Inoculation

SIR,—I learned the boiling petroleum jelly method of sterilizing needles (March 17, p. 543) in Sir Almroth Wright's laboratory in 1906, and in 1941 employed it with confidence and satisfaction in country schools for mass inoculations of children against diphtheria. Wright was a practical genius, and the simple outfit of a small enamelled bowl of petroleum jelly, a suitable support, and a spirit lamp has everything to recommend it nearly 50 years after it was introduced.—I am, etc.,

Staffordshire. A. G. COULLIE.

SIR,—The paper by Fleming and Ogilvie (March 17, p. 543) on the sterilization of needles used in mass inoculations apparently refers to intramuscular as well as subcutaneous injections. They mention the possibility of tissue fluid passing beyond the needle into the syringe and make this a reason for not drawing up more than one dose at a time, for any movement of the piston might cause this to occur. It should be the practice, however, when making any intramuscular injection, to withdraw the piston in order to ensure that a vein has not been entered. This practice would seem to be very likely to contaminate the syringe with body fluid even if only one dose has been drawn up, and thus constitute a danger from infection to later patients.

Whatever method may be used to sterilize the needles, to make mass inoculation completely safe a new sterilized syringe should be used in every case. This may be impracticable in some clinics, but it should be the practice in any hospital.—I am, etc.,

Sheffield. M. G. PHILPOTT

Cortisone and Toxaemia of Pregnancy

SIR,—I read your leading article (March 10, p. 517) with much interest. I quite agree that it is better not to stress too strongly the differences between glucocorticoids and mineralo-corticoids, because, as you wrote, cortisone and desoxycorticosterone have sometimes the same effect (oedema). I venture to draw your attention to the state of pregnancy, which in my opinion can give us valuable information about the functions of the adrenal cortex under natural conditions—or at least not experimental ones such as Selye has used. It is very well known that every pregnant woman is liable to retention of water and sodium; moreover, the cortex of the adrenals in pregnancy is hypertrophied (better, hyperplastic) and shows microscopically every sign of feverish action; in the last three months of pregnancy the excretion of 17-ketosteroids and 11-oxycorticoids in the urine is raised (Venning). Keeping in mind that patients who suffer from Addison's disease (in many respects the opposite of the state of pregnancy) become oedematous when they get too much desoxycorticosterone—e.g., by pellet implantation—together with salt infusions, it seems reasonable to accept that the retention of water and sodium in pregnancy has been caused by a hyperfunction of the adrenal cortex, stimulated by secretion of A.C.T.H. by the pituitary. Until a year ago it was impossible to prove this assumption, but by now a great many diseases have been treated with A.C.T.H., mostly with temporary success, but showing very regularly as so-called side-effects oedema, which can be controlled by reducing sodium in the food; hypertension; striae, acne, redness of the face, pigmentation, hirsutism; albuminuria (G. W. Thorn, *Arch. intern. Med.*, 1950, **86**, 319); convulsions, and death (L. J. Soffer *et al.*, ibid., 1950, **86**, 558).

This seems conclusive proof, because we have here under experimental conditions (A.C.T.H. injections) a hyperplasia of the adrenal cortex, as in pregnancy, and see that not only water and sodium retention appear, but that successively all the symptoms of even the severest forms of toxaemia show themselves. The main influence of the steroids which are released from the adrenal cortex in pregnancy seems to be that the capillaries in the whole body become more

permeable to plasma albumin, causing oedema in the subcutaneous tissues, albuminuria in the glomerular capillaries, and probably necrosis in liver, kidneys, and brain, by impairing at least in some places the circulation in the tissue spaces between cells and capillaries, which become gorged with serum and albumin. As is known, Parviaina *et al.* (*J. Obstet. Gynaec. Ludhiana*, February, 1951) showed with pregnant rabbits that the pathogenesis of desoxycorticosterone intoxication is very similar to toxaemia. Probably the aetiological factor which causes the enlargement of the adrenal cortex is a food factor. Selye showed that animals on a diet rich in casein (30%) get hyperplasia of the adrenal cortex; during the war, casein-rich food (milk) was very scarce even in Holland, and as a matter of fact the number of cases of toxaemia was in that period exceedingly low (mortality in 1944 was 1 in 5,000, before the war 1 in 3,000). To me the only possible conclusion is to regard the milk casein as an important aetiological factor in the pathogenesis of toxaemia.—I am, etc.,

Amsterdam. R. SCHUURMANS.

Oesophageal Spasm and Antihistaminics

SIR,—The antihistamine compounds have been used for symptomatic relief in asthma, dysmenorrhoea, spastic colon, and diverticulitis, as well as for their more widely known actions in allergic and paroxysmal rhinorrhoea, urticaria, and allied conditions. They are said also to oppose the acid response of the gastric mucosa to histamine (*British Encyclopaedia of Medical Practice Cum. Sup.*, 1950, **141**, 18–20). The following case suggests that they may be of use in treating a most distressing condition—oesophageal ulceration with associated spasm, a condition not infrequently met with in practice, occurring in 20 of 350 duodenal ulcer and 70 gastric ulcer cases among private patients seen by Sir Arthur Hurst (*A Textbook of the Practice of Medicine*, by F. W. Price, 1946, p. 383).

A married woman, aged 35 years, came under my care in June, 1950, giving a history of inability to swallow solid food, substernal pain after eating, regurgitation of undigested food, with loss of weight for over four years. Symptoms at first had alternated with periods of relative freedom, but had persisted continually for the last 12 months. In 1946 she had been investigated fully and oesophagoscopy had shown "marked oesophagitis with superficial ulceration." She had "wonderful" relief following that investigation, and believed afterwards that her ulcers had been removed during the operation. Conservative treatment with liquid diet and atropine and alkalis had been instituted, but relapse had occurred. Three years later in December, 1949, she was again completely investigated and oesophagoscopy showed a similar picture to that previously found. There was no particular response, and symptoms persisted despite conservative treatment.

On examination she was seen to be much underweight (6 st. 13 lb.—44 kg.), anaemic, and resigned. A milk diet (already followed) was continued, with alkalis and atropine in full doses. Six weeks on this regime resulted in little change, weight rose to 7 st. 1 lb. (increase of 2 lb.—1 kg.). Moreover, she did not feel any improvement. She was then given "elixir benadryl," 60 min. (10 mg.) before food. The following two weeks she reported improvement, though symptoms persisted to some extent. "Phenergan," 50 mg. thrice daily, was then prescribed. A week later she reported complete freedom from symptoms and, moreover, gained 3½ lb. (1.6 kg.) in that week. This improvement has been maintained.

Though success in this case may be entirely fortuitous, and coincidental remission cannot be excluded, it seems reasonable to attribute the improvement to the antihistamine compounds. Their effect in this case may be related to their actions as local anaesthetics relieving painful stimuli, the spasmolytic action (J. H. Burn, *British Medical Journal*, 1950, **2**, 691) relieving spasm of the cardiac sphincter, and possibly an antihistamine action reducing oedema. I think a more extensive trial of these compounds in cases of oesophagitis in which carcinoma, etc., have been excluded might be worth while, since temporary alleviations of the condition may produce prolonged relief after discontinuation of treatment.—I am, etc.,

Camborne, Cornwall. S. W. VIVIAN DAVIES

Value of Local Streptomycin

SIR,—Dr. R. P. K. Coe reported a case of "Instillation of Streptomycin into the Pericardial Sac in Tuberculous Pericarditis" (January 6, p. 18). I would like to report three cases of the use of local streptomycin.

Case 1.—A boy aged 12 was admitted on January 6, 1947, with a diagnosis of tuberculous effusion of the pericardium. He showed the typical signs of a chronic pericarditis, and when the pericardium was aspirated tuberculous pus was obtained. In spite of aspiration of considerable volumes on five occasions the pericardial effusion appeared to be persistent, and it was decided to try local and systemic streptomycin. The drug was difficult to obtain, as it was then strictly controlled by the M.R.C. The systemic dose used was 0.5 g. six-hourly for 19 days. Instillations in the pericardium were as follows: From May 10 to 16, daily aspirations and injections of streptomycin in the pericardial sac, using a dose of 0.25 to 0.5 g. in 10 ml. distilled water. From May 16 to 28 aspirations and instillation of streptomycin were done on every other day. The effusion appeared to respond very well, and after May 28 no further fluid was obtained.

The child appeared to do well for a few months, but gradually developed signs of cardiac failure from constrictive pericarditis. He was transferred for operation on December 3, and operated on in early 1948. The pericardial thickening was very marked and the stripping was done with great difficulty. The operation was successful and relieved the cardiac symptoms. The child died two years later from tuberculoma of the brain. On looking back, we think a longer systemic course of streptomycin would have made a great difference by controlling the pulmonary lesion.

Case 2.—Aspiration of a psoas abscess by the posterior approach before the pus starts tracking has not been mentioned in the literature. The first aspiration was done here in early 1948, mainly as a diagnostic measure.

A girl, 20 years old, was admitted on January 11, 1947, with a probable tuberculous spine (lumbar vertebrae 4 and 5), with a swelling in the right iliac fossa. Radiographs of the spine were not conclusive, and the tense swelling in the right iliac fossa raised some diagnostic difficulties. An aspiration was done for diagnosis; about 8 oz. (240 ml.) of pus were evacuated and tubercle bacilli found. The abscess did not refill. Since the first aspiration, psoas abscesses have been aspirated here on many occasions with great ease and without any complications. Local streptomycin and *p*-aminosalicylic acid (P.A.S.) have been used since the introduction of these new drugs, together with their systemic use. Some abscesses need only one or two aspirations, while others may need more. The technique used is as follows.

If the patient is in a plaster bed, the affected side is lifted out and supported by pillows under the pelvis and the chest, at an angle of about 30 degrees. The trunk is slightly arched to separate the costal margin from the iliac crest. A long needle is used, as it may travel 3–4 in. (7.5–10 cm.) before entering the abscess. The point of entry is just above the iliac crest, behind the lateral body line, so as to enter the broadest part of the abscess from behind. As the peritoneum is pushed forward by the abscess there is no danger of entering it before striking pus. Up to 20 oz. have been removed, and the pus invariably shows tubercle bacilli. Streptomycin, 0.25–0.5 g. in 2–5 ml. distilled water, is injected after the aspiration. In some cases 5–10 ml. 10% solution of P.A.S. has been used.

With the increased use of streptomycin in tuberculosis of the spine, it seems quite logical that any large collection of pus should not be left behind if the drug is expected to influence the bony lesions.

Case 3.—Tuberculous palmar ganglia are not very amenable to conservative treatment, and surgical excision is not easy and often not adequate. If used early, local streptomycin may bring about a dramatic improvement, as in the following case.

A boy, aged 16, had been treated for pulmonary tuberculosis and tuberculosis of the spine since the age of 8 years. He developed infection of a right compound palmar ganglion in July, 1949. A course of systemic streptomycin was started on September 4, but the ganglion showed no sign of settling down. On November 7 it was decided to aspirate the ganglion and use streptomycin. The needle was introduced above the upper limit of the swelling and about 7 ml. yellow viscid fluid with ill-formed fibrin bodies was aspirated. Streptomycin, 0.5 g. in 2.5 ml. distilled water, was instilled. This appeared to cause a slight local reaction and so the dose was reduced to 0.25 g. in 2.5 ml. Only three more aspirations and streptomycin instillations were

necessary. The ganglion subsided completely and the finger movements were quite normal. After each aspiration, the forearm and wrist were immobilized in a straight splint.

It appears that early tuberculous lesions, being vascular, are very amenable to the influence of streptomycin used systemically and locally.

I am grateful to Dr. Emrys Jones, physician superintendent, for permission to publish this letter.

—I am, etc.,

Cardiff. M. D. DESHMUKH.

Diaminodiphenylsulphone and Tinea

SIR,—My attention has been drawn to the letter of Dr. P. H. Birks (January 27, p. 191) reporting a case of tinea corporis cured with D.A.D.P.S. given orally, and I have been asked to comment on it.

There is ample evidence that D.A.D.P.S. is a potent chemotherapeutic agent, being many times more active than sulphonamides against Gram-positive organisms such as the streptococcus and pneumococcus *in vitro* and in animals. It is widely used in veterinary medicine; but in human beings it is being used only in leprosy and in tuberculosis. A study of its action in other infections is highly desirable. For this reason, Dr. Birks's report is of interest; it is unfortunate that my experience here does not support his findings.

I personally have been using oral D.A.D.P.S. for two and a half years in patients with leprosy, numbering several hundreds; in this part of Nigeria, many thousands of patients have been receiving this treatment for the last year. In these patients tinea corporis is commonly seen, and D.A.D.P.S. appears to have little or no action in preventing it or in curing it.

It is perhaps worthy of note that streptococcal and pneumococcal infections are very rare in our sulphone-treated patients; in fact I have not found one. Staphylococcal infections are common as well as tinea infections: gonococcal infections also occur.

The range of activity of D.A.D.P.S. is obviously limited, and this fact is likely to limit its use in medicine, but in suitable infections its activity is so great, its dose is so low, and its use is so simple and safe that it might have a sphere of usefulness apart from leprosy and tuberculosis. A dose of 100 mg. a day, which can be given at one time, appears capable of exercising the full therapeutic effect.

In acute and subacute infections, daily treatment would appear desirable, and it is quite safe, for toxic effects appear usually only after weeks of continuous treatment. For long-continued administration, as in leprosy, we find that twice-weekly treatment with doses rising slowly over several weeks from 100 mg. to 400 mg. is preferable. It appears safer, better tolerated, and no less effective than daily treatment, and it is of course much simpler and cheaper.

Dr. Birks's letter raises one or two points. Increasing the dose to 200 mg. a day in the second week is not always devoid of risk, particularly in ill-nourished patients such as Indian labourers. The claim that sulphone is concentrated in the skin has now been withdrawn by its author.—I am, etc.,

Uzuakoli, Nigeria. JOHN LOWE.

Hypertrophic Pyloric Stenosis in Adults

SIR,—In the *British Medical Journal*, 1948, **1**, 99, I recorded two cases, and since then I have had three more. As these differ in some particulars from the former two, I think that they will be of interest.

Case 1.—A housewife, aged 25, whose father had been operated on by me in 1928 for gastric trouble, complained of pain in the epigastrium with loss of appetite and of weight, gradually increasing for about a year. The pain was eased by taking food or drink, but woke her at night, when she took something to eat. She had a large excess of resting fluid with a definite stenosis of the pylorus. Radiologically the stomach was enlarged. There was no response to medical treatment over 11 months. At operation a large stomach was found and the pylorus was felt to be thickened. Partial gastrectomy was performed with a posterior loop Polya. The patient made an uninterrupted recovery.

On examining the fresh specimen the pylorus was found definitely thickened to about twice its normal thickness, there being a very clearly demarcated wedge-shaped sphincter muscle which showed some palisading. The pathologist reported: "Heavy diffuse chronic inflammatory cell infiltration of the mucosa of pyloric canal; no actual ulceration seen, however, in the tissue examined." There was no ulcer, and the condition was undoubtedly one of hypertrophic stenosis.

Case 2.—An engineer, aged 28, had 10 years' continuous dyspepsia, with epigastric pain coming on at intervals of a few months and lasting for a few weeks, not noticeably affected by food or alkalis. Radiography showed a normal-sized stomach emptying rather slowly, with evidence of hypertrophic gastritis. Test-meal showed a great increase in both free and total acidity. At operation the pylorus was felt to be much thickened and the adjoining 2 in. (5 cm.) of the stomach felt rather like a tube. The fresh specimen showed an immense thickening of the pylorus. The sphincter was well demarcated from the stomach muscle, and the sphincter muscle itself measured very nearly 0.5 in. (1.2 cm.). The muscle coat of the adjacent stomach wall measured just over 0.25 in., this thick region shading off gradually into the rest of the stomach. Palisading was not particularly marked. There was no evidence of past or present ulceration.

Note that both these patients were much younger than the two reported formerly. In the girl, who had the shorter history, the hypertrophy was slight, but one wonders if it would have gradually increased if operation had not been performed.

Case 3.—A woman was operated on for sub-acute cholecystitis. On examining the stomach the pylorus was felt to be very much thickened and the adjoining 2 in. or so of the stomach felt like handling a piece of hose-pipe. In view of the complete absence of any gastric symptoms and the general healthy look of the region, and the fact that it seemed to contract and relax normally, it was felt that there was no suggestion of malignancy, and the condition was left. The radiologist reported on a bismuth meal: "No organic lesion detected in the oesophagus or stomach. Initially some persistent pylorospasm but no evidence of an intrinsic lesion of the pylorus or abnormality of the duodenal cap. The gastric emptying time is normal." This case seems to show that the condition can occur in an apparently normal patient with no symptoms of gastric upset.

I should like once more to suggest that this condition is probably much commoner than is generally held—I am etc.,

London, W.1. A. J. HOBSON.

Congenital Abnormalities

SIR,—In 1904 J. W. Ballantyre wrote, "The embryo of the chick differs from that of the mammal in the details of its development. . . . This principle cannot be too clearly kept in mind; for in the past it has been neglected, and what was observed in the chick embryo was regarded as proven also for the human embryo, with results which were disastrous so far as accuracy was concerned."

Dr. P. K. Duraiswami is responsible for the following inaccuracies in his article (August 12, 1950, p. 384) and subsequent letters (*British Medical Journal*, 1950, **2**, 1002, and March 31, p. 704).

1. He states (August 12, p. 385), "The growth of the embryo as a whole is retarded to a degree varying with the dose of insulin" (dose 0.05 to 6 units), and, "By employing this technique I have observed that there is not only very marked stunting of the cartilaginous skeleton in the insulin-treated chick embryos as compared with the controls . . ."

Subsequently he has denied this (March 31, p. 704), quoting the same dose of insulin (0.05 to 6 units). The reliability of his statement is further weakened when we know that Lariste and Féré, at the end of the nineteenth century, used more than 40 different substances to produce deformity in chicks and invariably noted retardation of growth. Their experiments were rigidly controlled and large numbers of eggs were used (J. W. Ballantyne, *The*

Embryo, 1904, p. 217), which were allowed to rest in the dark beforehand. This is in contradistinction to the use of spirit by Dr. Duraiswami to "sterilize" the egg-shell.

2. He claims (August 12, p. 388) that his results are due to the specific action of insulin, and has not since rescinded this statement. Later (March 31, p. 704), "similar" claims are made for "synthalin," certain sulphonamide compounds, and thallium salts. Where, then, is the specific action of insulin? If this is not allowed, his discussion on hypoglycaemia becomes irrelevant, particularly as we know that "there are no cases known in which there is an absence of association between carbohydrate metabolism and early development [of the embryo]" (Joseph Needham, 1936, *Proc. roy. Soc. Med.*, **29**, 1593), and in all probability the occurrence of malformation in the organogenetic period is due to disturbance of the protein-carbohydrate evocator complex, produced in gross experimental work by many substances.

The absence of any action by insulin after the twelfth day (p. 388) indicates the end of the organogenetic period in the chick, following which insulin would have only a transient action as in the adult.

3. It is gratifying to note that the fallacy of comparing the chick with the human embryo has been realized (March 31, p. 704). I pointed this out (February 3, p. 247) following his letter of January 20 (p. 137), when obvious inferences were made regarding insulin-treated chicks and diabetic mothers. I only beg that this principle be carried further, as I did at the beginning of this correspondence; the ontogenesis of the chick is so utterly different from the human. One cannot seriously compare the chick deformity shown in Fig. 4 (August 12, p. 385) with club-foot in the human. Morphology alone demands greater accuracy.

4. There is a grave discrepancy between Dr. Duraiswami's interpretation of a certain specimen (August 12, 1950, Fig. 13, p. 388) and Mr. Bryan McFarland's interpretation of the same specimen (*J. Bone Jt Surg.*, 1951, **33B**, Fig. 33, pp. 45 and 46). The former states (p. 387) that it "shows a midsaggital section of the tibia from a 20-day-old insulin-treated *embryo* . . . special features to be noted . . . are the deformity, the pathological fracture, the *stunted growth*, and the lack of subperichondral ossification. . . ." (My italics.)

The latter states, "Fig. 33 shows one of the *chickens* in which defects in the tibia closely resembling the pseudo-arthrosis in children were produced."

Further, Mr. Bryan McFarland's composite Fig. 33 includes the picture of a chicken described in Dr. Duraiswami's article (Fig. 5, p. 386) as a *chicken 3 weeks old* showing bilateral dislocation of the knee in addition to pathological bowing of the tibiae. The chicken has no relation whatsoever to the accompanying section of an embryo, although the legend identifies them as the same.

Obviously little effort has been made to check what has been written before, a discrepancy difficult to justify in work of this nature.—I am, etc.,

Sheffield. GAVIN C. GORDON.

Treating Lumbago

SIR,—With diffidence I record a personal experience of a lumbar disk lesion and suggest a line of treatment which may be of value in certain types of cases.

After an over-flexion of the lumbar spine I experienced a slight backache which by the next morning had become a severe lumbago as described by Dr. J. Cyriax in his article in the *British Medical Journal* (December 23, 1950, p. 1434). The symptoms steadily worsened, and by the evening there was typical lumbar straightening and acute pain in the lumbar spine aggravated by walking or attempting to stand upright, the only comfortable posture being a position bent forward and to the left.

This would appear to indicate an increasing protrusion of nuclear material, but it is interesting to note that in at least five previous attacks over the past 25 years the onset had been initiated by a definite click in the back followed by agonizing lumbar pain with flexion fixation characteristic of abrupt cartilaginous displacement.

Bearing in mind the lucid explanation of the mechanism of the condition given in the article mentioned, I attempted the following reduction manœuvre, which, so far as I am aware, has not hitherto been described.

Assuming a full-length supine position on the floor, I clasped my hands and held them under the lumbar curve of the spine. A period of about five minutes' relaxation was given to allow for a reduction of muscular spasm. Efforts were then made to force the pelvis downwards over the fulcrum made by the hands. When the pelvis appeared to be touching the floor, first one leg, then the other, then both together were raised from the floor and a "cycle-pedalling" action was undertaken. After a return to and a short rest in the initial position, it was found possible to stand in an upright position with a completely normal and painless lumbar spine. This has remained so, but there were indications that no liberties could be taken with the recently reduced disk and great care had to be taken to maintain lumbar lordosis.

My only excuse for reporting this occurrence is in the hope that those with greater opportunities than mine may be able to assess the value, if any, of this simple therapeutic manœuvre. I am conscious of the statistical weakness and of the *post hoc ergo propter hoc* fallacy, but the immediate and dramatic relief personally experienced was in such sharp contrast to the marked discomfort and disability which accompanied five similar attacks that I am encouraged to hope that the method may have some merit.—I am, etc.,

Kensington, W.8. J. H. WEIR.

Anatomy of the Inguinal Canal

SIR,—There are certain issues of some anatomical importance in Mr. Walter Thompson's paper on the "Radical Cure of Inguinal and Femoral Hernia with a Polythene Insert" (April 14, p. 797) which may repay discussion.

With regard to the posterior wall of the inguinal canal it is not commonly realized that the transversus usually forms most of the conjoint tendon, although it is so stated in some of the older textbooks. In my own series of dissections I found that the transversus played the dominant part in this respect in 39 out of 58 canals, and in these 39 canals the transversus fibres reinforced almost all of the posterior wall of the canal and were intimately fused with the transversalis fascia. Therefore in most instances it cannot be possible to make any incision transversely from the deep inguinal ring in the posterior wall of the canal, and of greater length than 0.5 in. (1.3 cm.) at the most, without dividing part of the conjoint tendon.

My dissections have also shown that the cremaster exhibits certain definite attachments to the posterior wall of the canal, and in particular that there are fibres inserted close to the medial side of the deep inguinal ring which, in the normal inguinal canal, are probably concerned with the approximation of the margins of the ring. In Mr. Thompson's cases the cremaster was excised, and I raise this point lest occasionally a potentially useful muscle be sacrificed.

Mr. Thompson states that the sphincter mechanism of Sir Arthur Keith is left intact, but it is later said that the new deep inguinal ring is displaced laterally for 1 in. (2.5 cm.) deep to the transversus. Having in mind this fact, and that a 3.5 in. (8.8 cm.) plate of polythene has been sutured in the inguinal canal, may I say that it is hardly likely that a sphincter mechanism, or indeed any other physiological mechanism, could operate after the extensive manœuvres employed?

Mr. Thompson condemns Lockwood's repair for femoral hernia "in those patients who might be expected to have a preformed oblique sac." One would like to know on what criteria this expectation is based, as there will not usually be a history of hernia on the other side or of imperfect testicular descent. If there is no definite evidence of inguinal hernia how may a preformed sac be expected?

I put these points in no way criticizing Mr. Thompson's operation but as anatomical considerations which it may be worth while taking into account.—I am, etc.,

London, W.C.1. MICHAEL J. BLUNT.

Typhus and Typhoid

SIR,—In his interesting article on "A Century of Physicians" (March 24, p. 636) Sir Henry Bashford states that William Jenner was the first to proclaim typhus and typhoid fever as separate entities. Surely this is incorrect. Credit for first distinguishing these diseases is generally given to W. W. Gerhard, of Philadelphia, who published a lucid article on the subject in 1837 (*Amer. J. med. Sci.*, **20**, 289). He gave an excellent description of cases of typhus fever which he and Pennock had observed in an epidemic during the previous year, and clearly differentiated the disease from typhoid on clinical grounds. As C. Murchison stated in a letter to the *Medical Times and Gazette* in 1857 (n.s. **15**, 642): "The truth is, that, as in most discoveries, the steps towards the recognition of these distinctions have been gradual. . . ." Murchison pointed out that in 1822 a certain Dr. H. Autenrieth, a young German physician studying in Edinburgh, had published a paper in the *Edinburgh Medical and Surgical Journal* (1822, **18**, 325) "On the Spasmodic Abdominal Typhus of Young People" which he had observed in Germany; the symptoms were evidently those of typhoid, and Autenrieth clearly considered it as different from typhus. Murchison also mentioned that Perry and A. P. Stewart, of Glasgow, and H. C. Lombard, of Geneva, had recognized the differences between these diseases by 1836. As so often happens with scientific advances, the same conclusions were evidently reached by several observers about the same time.

Sir William Jenner's contribution occurred later. He made a careful study of the symptoms and pathology of the two diseases from 1847 onwards, and incidentally contracted both infections in doing so. He first published his conclusions on the non-identity of these fevers in 1849–50 (cf. *Lectures and Essays on Fevers and Diphtheria*, 1849–79. London, 1893). According to Murchison he advanced the subject by endeavouring to show, first, that the same focus of contagion would produce only one kind of fever, or that each would communicate only itself and not the other; and, secondly, that an attack of either fever produced immunity from subsequent attacks of itself but not of the other.—I am, etc.,

Whitechapel, E.1. H. G. DUNN.

Confidential Papers and the State

SIR,—The Ministry of Health has informed hospital authorities that they can properly loan patients' case records for the use of the Ministry of National Insurance and the Ministry of Pensions, and instructed them that these records should be provided on request. It is clear that the matter of medical confidence, and how it may be preserved, has been considered—an attempt is being made to observe certain safeguards—but on careful reflection it becomes apparent that the question has much deeper implications, and is one that involves fundamental principles.

While it is stated that "case papers will be treated as confidential" the circulars go on to make reservations which could only undermine the whole basis of that confidence between patient and doctor which has obtained unchanged for many hundreds of years as a vital element of that relationship and as a fundamental principle of our professional faith. An example of this is the statement, in the circular relating to the Ministry of National Insurance, that "the regional medical officer may find it necessary to make extracts of the relevant portions of the case papers which have been taken into account by the medical boards in their examinations. . . . The patient will not be put in possession of any information *other than the extracts mentioned above* which are directly relevant to his claim, and if these extracts contain any information which might be harmful to the claimant the regional medical officer will take care to give it only to the claimant's own doctor or, as appropriate, *to his trade union or legal representative*" (italics mine). Another example is the statement of case prepared in connexion with appeals to Pensions Appeal Tribunals, statements which must legally be made available to both sides.

The intentions are doubtless excellent, but in medical confidence, as we have always known it, there can be no reservations. A medical history, or notes of an interview with a patient, are either completely confidential or they are not confidential at all. It is within the experience of the writer that the practice of loaning case records to Ministries is leading to results that are highly undesirable both for patient and doctor.

Consider the patient's standpoint. Can we assure him that what he says will be regarded as confidential? If not, it is our duty to make this clear, in fact to "caution" him. Will he be so frank with us then? Or, take the doctor's standpoint. Is it right that confidential notes and opinions, including those taken before July, 1948, should be revealed to the patient and others? Of far greater importance is the danger to the patient (acknowledged by the Ministry of Pensions) of learning facts which may have an untoward effect on him—for example, that he is suffering from schizophrenia, and that the prognosis is unfavourable. And in practice, despite the safeguards, this unhappy consequence occurs not infrequently. Where other than medical personnel are involved, could we fairly expect otherwise? It is small wonder that it is becoming increasingly common for new patients to ask whether the interview is confidential, or to request that written notes of their story shall not be made.

Incidentally, in the event of a patient refusing his consent, would he prejudice his case thereby? What might be the consequences were the hospital or the medical staff concerned unable to see their way to comply? Do the regulations governing the issue provide safeguards for these eventualities?

Ways of evading the problem which may suggest themselves are not worthy of consideration. Our duty to our patients demands that the Ministries shall receive all the help we can give, and it is hard to see how a case sheet to which neither patient nor doctor has contributed frankly, an "expurgated edition," could be of assistance. A positive attitude on our part is essential. Could not a Ministry ask for information about an individual patient (consent having been freely given) and the doctor comply in the form of a report? Its contents would then be a matter for the discretion of the doctor concerned, and if the report could be regarded as absolutely confidential it would doubtless be more helpful to all parties. Another alternative might be to submit the case to independent and authoritative medical opinion, though again the report would need to be confidential if it is to be of value. (The latter procedure has for some years obtained in cases submitted to H.M. Treasury Referee.) Most helpful of all would be for this important subject to be fully ventilated in your columns, with the usual free and unfettered expression regarding experiences and views.

It might be tempting at this stage once again to try to salve one's conscience with the argument that the procedure advocated by the Ministry of Health is the law, and that we are powerless to alter it. But to the doctor–patient relationship there are two parties; and whether the public, who make the laws, would, if they were apprised of the true position, willingly forfeit their traditional privileges under that relationship seems doubtful. Medical confidence admits of no compromise. To guard against infringement or subtle change of emphasis demands our constant vigilance.—I am, etc.,

Liverpool. S. BARTON HALL.

The South African Meeting

SIR,—The attention of my council has been drawn to Dr. Ralph Lawrence's letter in your *Journal* of March 10 (p. 530) in which he describes an incident when he was a medical student at this university. This was discussed at a meeting of the Medical Students' Council on April 4, and the following resolution was passed *nem. con.*: "This council, the representative body of the medical students of the

University of Capetown, regrets the treatment received by Dr. Lawrence, and records its opposition to any form of discrimination against students." It was further decided that a copy of this motion be sent to the *British Medical Journal*.

The facts mentioned by Dr. Lawrence are substantially correct. However, probably very little can be done to remedy the present situation, as the factors involved are not those which apply to an isolated case, but lie in a far wider province. Nevertheless, the Medical Students' Council, which has only just been formed, proposes to discuss the position in greater detail and will try to do what it can to see that every student has the fullest opportunity to benefit from his medical education.

In conclusion, it must be stressed that the Medical Students' Council does not claim to speak for the University, but only for the students whom it represents.—I am, etc.,

Capetown. E. A. ALLEN,
Secretary, Medical Students' Council.

POINTS FROM LETTERS

Etiquette

Mr. GEOFFREY MYERS (London, W.1) writes: When I was a student, twenty years ago, it was taught to us, *en passant*, that elegance demanded a certain formula being adopted in the authorship of medical articles submitted to the medical literature, that form being that authors should be named in alphabetical order and never in order of age, professional seniority, or for any reason other than alphabetically. It is therefore with some measure of nostalgia for the days when form meant something that I notice now, in every issue of this and almost every other medical periodical, a departure from that highly commendable tradition. An article by Brown and Walters (using entirely fictitious names) should state that it is by Brown and Walters, and never by Walters and Brown, merely because Brown happens to be a registrar while Walters is his chief. Abrahams and Murray (again fictitious) should remain Abrahams and Murray, and not become Murray and Abrahams because Murray happens to be the President of the Royal College of this or that. . . . I once heard it said (and have always practised it myself) that upon acquiring hospital staff status one should address one's staff colleagues by their surnames without any prefix, the exceptions being those sufficiently well known to be called by their first names. I have, however, not found that this is a generally adopted procedure in all hospitals. Perhaps it would be well if it were.

"Anthisan" in Whooping-cough

Dr. L. SHELDON (London, N.W.10) writes: A little boy aged 4 years developed an urticarial rash during the third week of whooping-cough. Anthisan 0.05 g.—one tablet three times a day—was ordered. Much to my surprise, the cough reflex was completely abolished for 48 hours, and during this period the boy had two convulsions. His lungs fortunately remained clear throughout. He was given "cremomerazine" as a precautionary measure, and an expectorant mixture, and during the next 24 hours had seventeen paroxysms of coughing.

Correction.—The authors of the paper, "Two Cases of Simmonds's Disease" (April 28, p. 924), much regret that inadvertently no acknowledgment was made to the department of pathology, Reading area, for the great help and large number of investigations made on these two patients.

Sweden and New Zealand lead world statistics of the lowest rates of infant mortality, according to a report issued by the World Health Organization. Iceland, Holland, and Australia come next. Not only an indicator of the state of child health but also of that of the whole population, the figures show a rate of mortality of 23 per 1,000 infants in Sweden under the age of 1. Corresponding figures for the United States are 31, Britain 32, Denmark and Switzerland 34. Comparative figures for child mortality to-day and 50 years ago indicate that the rate has been steadily declining since the beginning of the century. In Sweden it has decreased from 98 to 23, in Belgium from 172 to 63, in Spain from 186 to 64, and in Australia from 104 to 28.

Obituary

Sir ALBERT COOK, C.M.G., O.B.E. M.D.

Sir Albert Cook died at Kampala on April 23 at the age of 81, after a long and distinguished career devoted to the people of Uganda.

Albert Ruskin Cook was born in London, the son of the late Dr. W. H. Cook, of Hampstead, and was educated at St. Paul's School and Trinity College, Cambridge. At both these seats of learning he swept the board of scholarships and prizes. After taking the B.Sc.(London) he gained a first class in both parts of the Cambridge Natural Science Tripos. At St. Bartholomew's Hospital, where he was Shuter Scholar, he graduated M.B. in 1895. He could then, with the ball at his feet, have become a Harley Street consultant if he had wanted to, but he elected in 1896 to go to the infant Protectorate of Uganda for the Church Missionary Society. In those days there was not a road in East Africa of any kind other than native paths, nor any form of transport other than human, and Cook and thirteen other young missionaries trudged the whole 850 miles from the coast to Kampala through country where some of the tribesmen were still resentful of white domination—though the most truculent of them, the Masai, had learned a lesson at the hands of the bloodthirsty German, Karl Peters, not many years before. The only woman of the party, Sister Katharine Timpson, of Guy's Hospital, later became Cook's wife. On reaching Kampala Cook opened his medical practice in a disused smithy, but soon the first buildings of Mengo Hospital were erected, 141 patients being admitted during the first year. The Uganda Mutiny broke out very shortly after his arrival, and during its suppression by Macdonald and a small force of British officers and men Cook's services to the sick and wounded were invaluable.

About that time he was joined by his younger brother, John Howard Cook, M.S., F.R.C.S., who died in 1946 (*Journal*, 1946, **2**, 519). The two brothers in 1901 were the first to diagnose sleeping sickness in East Africa, and they rendered an immense service to the development of civilization in that country by providing medical and surgical care of the very highest class to the Baganda (the inhabitants of Uganda) and to European officials, soldiers, settlers, and traders. When fighting broke out in German East Africa in 1914 Mengo was the only hospital of any standing in Uganda, and it became the base hospital in the Lake Victoria region under Cook's superintendence. He and his wife were tireless in their attention to the sick of all races who poured into the hospital. In 1917 Cook founded the first school for African medical assistants in Uganda, and the following year the deep concern which he shared with his wife for maternity work and child welfare was demonstrated by the founding of a maternity training school, from which graduated the first qualified African midwives in Uganda. Cook's organizing and medical abilities were devoted to his hospital, which by 1931 was the most up-to-date in the country. The Baganda, who had developed a certain civilization of their own before the advent of the white man, warmly appreciated the benefits which European medical science had to offer through the brothers Cook, and the work at Mengo went steadily from success to success. The younger

brother eventually returned to England, but when Albert retired in 1934 he remained in Uganda. By that time Mengo Hospital had many branch dispensaries, a maternity training school with several branches, a medical school, and a nurses training college. Patients came to consult Cook at Mengo from as far afield as India and South Africa.

The list of his appointments is impressive: consulting physician to the European Hospital, Kampala, and to the Mengo Hospital; vice-president of the Church Missionary Society; president of the Uganda Branch of the B.M.A.; president of the Uganda Literary and Scientific Society; mentioned in dispatches for service in the Uganda Mutiny, and again for war service in Uganda from 1914 to 1917; O.B.E., 1918; C.M.G., 1922; silver medal of the African Society, 1928; Knight Bachelor, 1932; representative of Uganda at the Coronation, 1937; Croix de Chevalier de L'Ordre de Léopold. But all these honours never dulled his sense of vocation. He was always first and foremost a missionary, and Mengo has always been in the fullest sense a mission hospital. Sir Albert Cook spent his retirement in Uganda among the people he loved so well. In collaboration with Lady Cook, who died in 1938, he published a handbook of midwifery in Luganda (the language of the Baganda) as well as a medical vocabulary and phrase book. His volume of *Uganda Memories* appeared in 1945. The death of "Cook of Uganda" removes from the scene of his labours a man worthy of mention alongside Livingstone himself among the great Englishmen and missionary doctors of modern times.

Dr. ARCHIBALD NEVILLE MCLELLAN, consulting gynaecologist to the Victoria Infirmary, Glasgow, died in Liverpool on March 5. He studied medicine at Glasgow University, graduating M.B., C.M. in 1894. Developing an early interest in gynaecology, he took the L.M. (Rotunda) in 1896. For some time he was a demonstrator in the anatomy department at Glasgow University and prided himself on his knowledge of pelvic anatomy, which later stood him in good stead in the surgery of the pelvis. For over 30 years he was on the staff of the Royal Maternity and Women's Hospital, Glasgow, and for a similar period was gynaecological surgeon to the Victoria Infirmary. He took a great interest in university teaching and for many years was assistant to the professor of midwifery, the late Professor Murdoch Cameron. An internal examiner in midwifery and gynaecology to Glasgow University, he was also an examiner to the Central Midwives Board of Scotland. In 1929 he was elected a Fellow of the Royal College of Obstetricians and Gynaecologists.

Professor R. A. Lennie writes: A most able clinician and meticulous operator, McLellan had ample opportunity of demonstrating his surgical skill, more especially as in his early days gynaecological surgery was in its infancy. He kept well abreast of the times and welcomed any new technique or surgical procedure. His operative results were excellent, and he had the confidence of a large circle of practitioners in the south side of Glasgow. He was much beloved by his patients, colleagues, and friends, being a most kind and courtly gentleman, with whom it was a pleasure and privilege to be associated. He was of a retiring disposition and had few outside interests, though he was interested in music, and in his declining years derived much personal pleasure in composing new settings for many of the old Scottish songs and ballads. He reached a ripe old age and was gracious to the end. He belonged to an era of medicine where voluntary service, tradition, and kindliness were accepted qualities—and these he possessed to an outstanding degree. In his death, medicine has lost one of the finest members of the older school.

Dr. EUSTACE JOHN PARKE OLIVE, consulting physician to the Warneford Hospital, Leamington, died suddenly on April 14 aged 88. He had a distinguished career as a student at St. John's College, Cambridge, and St. Bartholomew's Hospital. After graduating M.B., B.Chir. in 1889, he held house appointments in his own hospital and then migrated to the General Hospital, Birmingham, where he was house-surgeon to Gilbert Barling. In 1892 he took the F.R.C.S., and two years later proceeded M.D. About this time he went to Leamington, where he was appointed to the staff of the Warneford Hospital, and spent his long life of professional service in that town. During both world wars he was actively employed, being awarded the O.B.E. at the end of the first. Always ready for emergency work, in his later years he equipped himself as a very competent anaesthetist. He led a full and valuable life and earned the gratitude of many.

Medico-Legal

DOCTOR'S ACTION AGAINST HOSPITAL BOARD TO PROCEED

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On March 28, 1951, the First Division of the Court of Session in Edinburgh allowed an appeal[1] against a decision given by Lord Sorn in November, 1950, dismissing an action against the Greenock and District Hospital Board by Dr. John Walker, of Broomhill Avenue, Glasgow. Dr. Walker's case is that in June, 1947, the board agreed to appoint him resident physician-superintendent of the Gateside Infectious Diseases Hospital, but in October, 1947, refused to appoint him. He had meanwhile held himself free from other commitments. Dr. Walker claims £8,000 damages for breach of contract.

By the defence the board contends that it was a condition of the agreement that it should be confirmed in writing, but that it never was so confirmed; that written evidence of the contract, being a contract for more than a year, was required, but that Dr. Walker did not allege there was any; that the board was induced to enter into the agreement by false and fraudulent misrepresentations by Dr. Walker; and that the action was barred by Section 166 of the Public Health (Scotland) Act, 1897, which protects authorities from liability in damages for their *bona fide* acts in execution of their statutory duty.

In allowing the appeal and sending the action for trial the Lord President, Lord Cooper, dealt with the board's allegation of fraudulent misrepresentation against Dr. Walker. The board's case was that he had not disclosed that in 1942, after a Ministry of Health inquiry, he had been dismissed from the office of county medical officer of Northumberland. It was common ground that afterwards he had held the appointment of chief medical officer to the County of Zetland until 1944.

The Greenock post, carrying a basic salary of £900, was obviously different in character from that of chief medical administrator of a large English county. Lord Cooper could not see why failure in such a capacity in 1941 should necessarily or probably imply incapacity for the Greenock post in 1947, and the apparent attitude of the Board that Dr. Walker was thereby permanently disqualified from holding any post in the service of the public health authority, however small the post might be, was wrong. The board's forlorn attempt to argue that the contract had been broken in the public interest was untenable. Accordingly the action must be sent to proof.

[1] *Manchester Guardian*, March 29.

Medical Notes in Parliament

Mr. Bevan's Statement

In the course of his statement to the House of Commons on April 23, after his resignation from the Government, Mr. ANEURIN BEVAN said his quarrel with his colleagues was not based solely on what they had done to the National Health Service. But, if the Chancellor of the Exchequer found it necessary this year to mutilate the Health Services for £13,000,000, what would he do next year? He asked why the National Health Service should be thrown away. Had the American Medical Association succeeded in doing what the British Medical Association failed to do? He was entitled to answer the accusation that he had agreed to a charge for prescriptions. He had known that charge would never be made, because it was impracticable, and it was never made.

Health Service Bill

Mr. HILARY MARQUAND, on April 24, moved the Second Reading of the National Health Service Bill. He said that when the Secretary of State for Scotland and he framed their estimates for this year they found that, if the full estimates presented by the regional hospital boards were accepted, £30m. more would be required than in last year's estimates. That was mainly because of the rise in the cost of hospital services, which accounted for roughly 60% of the total cost of the National Health Service. Other increases resulted from the influenza epidemic and the increased cost of drugs, especially imported drugs, but were more or less offset by savings elsewhere. Members on both sides of the House continually drew attention to the need for more beds for chronic sick, gynaecological cases, and other deserving groups. The Government was making provision for more accommodation and beds, hoping that improved conditions would bring forward more staff. In particular it was making greater provision for treatment of tuberculosis. In 1950 for the first time tuberculosis notifications had fallen, despite the detection of unsuspected disease by mass radiography. Since the start of the National Health Service, over 3,500 additional beds had been made available for treatment of tuberculosis in England and Wales, and he aimed this year to provide 2,000 more. About 150 beds for England and Wales and the same number for Scotland would be provided in Switzerland as authorized in Clause 3 of the Bill. England and Scotland undertook an experiment of equal size so as to compare results. In the future hospital facilities were to be expanded, and there must also be better facilities for the group practice of medicine by general practitioners, although it was at present impossible to establish large numbers of health centres. For all these purposes more money was needed than the Chancellor could see his way to provide. The estimates required £30m. more for maintenance and expansion of essentials. The Chancellor could not provide more than £7m. Therefore £23m. must be found within the Service. The general-practitioner and hospital services accounted for some 75% of the total expenditure. Out of the remaining 25% £23m. had to be saved.

Economies had already been made by Mr. Aneurin Bevan, such as the cuts in the remuneration of dentists, ophthalmic opticians, and ophthalmic medical practitioners, and in the chemists' allowance for prescribing. He said that after considering the problem he had decided to reduce the hospital estimates by £10m. No more could be done there, and it was necessary to obtain money from some other parts of the Health Service so that essentials could be maintained. The charges now proposed were estimated to yield £13m. this year, so that £15m. more could be spent on hospitals this year than last. In a full year the charges should yield £25m., and thus, despite the ceiling of £400m., there would be £12m. more available to meet essential needs and rising costs. A prescription charge, even if it did not exempt children, would yield only £6m. Mr. Marquand said he also rejected the so-called hotel charge in hospitals. If there had to be a charge, the best was one on appliances, not on treatment or services, and the only appliances which could satisfy his demand in full were dentures and spectacles. No charge need fall on children or on expectant mothers, and there would be no charge for treatment. The service had already supplied 20 million pairs of spectacles. Charges at present varied from nothing to 15s. 1d. per pair, but even so there was some evidence of abuse. There was to be no charge for in-patients in hospital, nor for spectacles in children's frames, nor for testing and examination of the eyes. The charge would not fall on those who were ill.

Sir HUGH LUCAS-TOOTH asked whether the resources available were being spent on really essential parts of the Service or were wasted in part. By taking off all charges over the whole Health Service, Mr. Bevan had taken the brake off demand before there was any possibility of adequate supply. Too many patients were chasing too few doctors, dentists, and hospital beds, and the result was damaging both to the national finances and to the Health Service itself.

Dr. SANTO JEGER said he had searched the Bill, but had found no reference to its proposals being temporary. Mr. Marquand had said that no demands were made upon the sick for any payments, but the Bill merely exempted in-patients of hospitals from payment of charges, and they were not the only people who were sick. He said that under the National Health Service the waiting-lists in opticians' consulting-rooms had been greatly reduced and the number of tests for eye defects had fallen. Turning to the question of dentures, he said any doctor would agree that it was already difficult to persuade people that they needed dental treatment, and the new charge was a deterrent. A lot could be done to bring down the costs of dental materials and the cost to the National Health Service if steps were taken to deal with the monopoly in them.

NEED FOR REORGANIZATION

Dr. CHARLES HILL said that, if the House took the line that sickness and its treatment came before anything else, they would come to a level of expenditure which would ruin other social services. One of the reasons for the present situation was that the financial and administrative structure devised for the Service provided insufficient control and economy within it. Money should be allocated at the lowest possible level, and those appointed to administer hospitals or groups of hospitals should be free to spend within those limits. Dentists would be just as busy after this Bill became an Act as before. He asked whether the proposed charge was part of an effort to restore the former efficiency of the school dental service. Parliament had not faced with sufficient candour the fact that there were not enough dentists to provide a comprehensive service. The Minister had not referred to the fact that the supplementary ophthalmic service was temporary. Not a word had been said of the promise that this kind of work should be done by and under the aegis of hospitals. Money could thereby have been saved while the Service was made more efficient.

Dr. H. B. W. MORGAN said the Health Service was a national service and based on egalitarian lines—not the sort of thing they were accustomed to in Tavistock Square. In the early years the cost of the Health Service was high, but gradually that would level down, as would the cost of the dental and ophthalmic services. He had been on the Council of the B.M.A. for 15 years and liked the fellows there, but they worked against anything progressive except what the medical profession thought it wanted. None of the teaching schools taught the rights and needs of the public; they contemplated more the rights and needs and comfort of the doctor.

Sir AUSTIN HUDSON, speaking of the tuberculosis proposals in the Bill, said reference was frequently made to the word "respiratory." The Minister had told him he was unwilling to take out the word because he did not wish to open the door too wide to the many types of tuberculosis. One particularly sad case was that of ocular tuberculosis, and the

only place where sufferers could get treatment was Switzerland. The N.A.P.T. had been able to send nine cases to Switzerland, but that was not satisfactory, and the Ministry was setting up a small hospital at Swanley in Kent to deal with such cases. That hospital would have only 22 beds, whereas the number of cases was 50 or more a year. He urged the Minister not to close the door against sending these people to Switzerland even when the Swanley hospital was open.

Mr. W. GRIFFITHS said that the timing of the Bill's introduction was extremely bad, as the services were being used with increasing discretion. The number of sight-tests was increasing at the moment because people wished to get in before the Bill became law. When it became law, many people would be worse off than they had been before the National Health Service was introduced.

Mr. P. L. E. SHURMER said the peak in the demand for spectacles and dentures had passed. On Clause 3 he remarked that it was not shortage of accommodation in sanatoria but shortage of nurses which hindered treatment of tuberculosis. He welcomed the Bill for its provision of treatment for tuberculous cases in Switzerland.

GOVERNMENT REPLY

Mr. HECTOR MCNEIL said the reason why Clause 3 was confined to respiratory tuberculosis was because the Ministry must tackle the infectious side of the disease, which meant the respiratory cases. Cases would be chosen primarily upon medical advice on their suitability for treatment, and the choice would be guided against cases where there was any expectation of surgical intervention of a major kind. The Ministry would try to aim at the case where the normal expectation of treatment was about six months. Payment would be made direct by the National Health Service to the sanatorium chosen. Mr. McNeil remarked that there had been charges from the beginning of the Health Service for a great range of services. The introduction of the dental charges could help towards filling the deficiencies in the school dental system. Before the Health Service came into operation, about 50% more dentists than at present were in the dental educational system. The drain-off had been almost exclusively to the National Health Service. The Government had made a decided movement towards better control of prescribing, mainly on the recommendations of the Cohen Committee. He promised to deal with other points during the Committee Stage, and said the Bill was not a breach of the Health Service but a conception inherent in the Act from the beginning.

The Bill was then read a second time without a division.

Teeth and Spectacles for the Forces

In answer to a question on April 24 Mr. J. STRACHEY stated that since the introduction of the National Health Service soldiers had been entitled to free teeth and glasses like other members of the population, and the question whether they would be affected by the new proposals for payment for these appliances was now under consideration.

Health Insurance in Malaya

On April 25 Mr. S. S. AWBERY asked the Secretary of State for the Colonies what steps were being taken to introduce a system of health insurance and social security in Singapore and Malaya. Mr. T. F. COOK replied that the introduction of such a system there was at present impracticable, but the medical services were being improved and extended. In Singapore it had been possible to provide free treatment in hospitals, free tuberculosis treatment, and family allowances for those under treatment. In the Federation of Malaya all workers were entitled to free treatment under the Labour Code, and it was given in the case of hardship in all Government hospitals. In Singapore a Working Party was investigating the possibility of introducing a scheme of social security.

Brussels Treaty Public Health Committee

In answer to a question on April 25 Mr. KENNETH YOUNGER said that this was one of several committees which would be considering the development of the social services of the five countries signatory to the treaty. It was composed of administrative and medical officers of the health administrations of the five countries and had been discussing the control of foodstuffs and proprietary medicines and the protection of health in wartime. The main result so far had been the union of the five countries into one for the health control of sea and air traffic.

Health Centres

On April 26 Dr. SOMERVILLE HASTINGS asked the Minister of Health how many health centres had been provided since July, 1948, and how many were now under construction. Mr. H. MARQUAND replied that nine premises taken over when the National Health Service began were being administered as health centres for groups of doctors and other services. One large centre was under construction and tenders for two smaller ones had been invited. Asked why he had refused the London County Council permission to provide a centre for group practice at the Hampstead Health Institute, the Minister said that the area was already well supplied with doctors and surgeries.

Tea Ration for Invalids

On April 23 Mr. J. A. LANGFORD-HOLT asked the Minister of Food whether he would provide an extra tea ration for chronic invalids.

Mr. F. WILLEY replied that on matters of this kind the Minister took the advice of the Food Rationing (Special Diets) Advisory Committee of the Medical Research Council, who thought that no medical condition required extra rations of tea for its treatment.

Mr. LANGFORD-HOLT pointed out that his question did not relate to the medical condition but to the fact that a cup of tea was one of the few pleasures a chronic invalid could get. He asked whether, since it did not mean the use of much tea, the Minister would reconsider the whole question.

Mr. WILLEY said he thought they ought to accept the advice of those best able to advise.

Hospital Charges

During the debate on the Adjournment on April 24 there was raised the case of a woman admitted to King's College Hospital for an emergency operation and who had been charged throughout as a private patient. Mr. A. BLENKINSOP drew attention to the fact that the Health Service Act said that pay-beds might be used without charge where there was urgency and no other accommodation was available. He said that during the past six months King's had admitted 65 cases to pay-beds without charge under this part of the Act. He emphasized that the hospital had always been willing to consider doing this, and also had amenity funds to help people who could not pay the full charges, provided the patient raised the matter straight away.

In answer to a question on April 26 Mr. H. MARQUAND said that about 6,875 beds, or 1½% of all staffed beds, were pay-beds in Health Service hospitals.

Mental Defectives.—On January 1, 1951, there were 5,316 mental defectives awaiting admission to institutions. Consolidation and amendment of the Mental Deficiency Acts are receiving active attention.

Hospital Accommodation.—The total number of staffed beds in hospitals now in the National Health Service was 440,231 on June 30, 1948, and 458,363 on December 31, 1950.

Trade Mark on Glasses.—The letters "N.H." are stamped on the two parts of N.H.S. spectacles, which are often made and sold separately, and are to ensure the quality.

Hearing-aids.—Just over 1% are returned as unsuitable.

Spectacles and Teeth.—5,950,000 patients have been supplied with dentures since 1948, and 17,000,000 pairs of spectacles have been issued.

Universities and Colleges

UNIVERSITY OF OXFORD

Robert Victor Coxon, M.D., F.R.C.S., has been appointed to the Readership in Human Physiology for seven years from October 1.

UNIVERSITY OF CAMBRIDGE

Professor James Dixon Boyd, M.Sc., M.D., Professor of Anatomy in the University of London, has been appointed Professor of Anatomy in the University of Cambridge, in succession to Professor H. A. Harris, who retires from the Chair on October 1.

C. M. Fletcher, M.D., F.R.C.P., has been appointed a member of the Court of Governors of the University College of South Wales and Monmouthshire from May 5, 1951, to May 4, 1956.

Professor R. A. Peters, M.D., F.R.S., Whitley Professor of Biochemistry in the University of Oxford, has been elected to an Honorary Fellowship of Gonville and Caius College.

UNIVERSITY OF ABERDEEN

The following medical degrees were conferred on April 5:

M.D.—*Valerie A. Cowie (née Field), *Helen L. D. Duguid, G. B. Forbes, A. A. White.

M.B., CH.B.—G. Adams, R. A. Andrew, B. M. Barron, G. W. Cruickshank, J. G. Donald, R. H. Duncan, J. A. G. Elmslie, Mair L. Jones, R. A. Kirton, Mary R. Kramer, Hectorina Matheson, June M. Oliver, Moira K. M. Pratt, Isobel B. A. Shivas, W. Soutter, I. D. Spark, R. A. Spark, B. S. Stephen, J. G. Sutherland, Dorothy M. McI. Sweenie, Jean P. Watson, Marjory I. K. Watt, R. M. Youngson.

The following prizes were awarded in the Faculty of Medicine: *Chanock Gold Medal in Anatomy*, W. M. Easson and M. J. Emslie (equal). *Durno Prize in Anatomy*, J. K. Finlayson; *proxime accessit*, M. J. Emslie. *Dyce Davidson Gold Medal in Materia Medica*, J. G. Fraser. *Fife Jamieson Memorial Gold Medal in Anatomy*, M. J. Emslie; *proxime accesserunt*, W. M. Easson and M. J. Williams. *Lizars Gold Medal in Anatomy*, J. K. Finlayson. *Ogston Prize in Surgery*, G. A. F. R. Grant and L. Symon (equal).

*With commendation.

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a quarterly comitia of the College held on April 26, with the President, Dr. W. Russell Brain, in the chair, the Rt. Hon. Winston Leonard Spencer Churchill, O.M., C.H., F.R.S., was elected to the Honorary Fellowship of the College.

Election of Fellows

The following were elected Fellows of the College: H. H. Stewart, M.D. (Belfast); B. A. Hunt, M.D. (Australia); W. G. Patterson, M.D. (Newcastle-upon-Tyne); B. F. Russell, M.D. (London); M. A. Ibrahim Bey, M.D. (Egypt); C. E. Dolman, M.B. (Canada); C. J. Hackett, M.D. (Middlesex); R. T. Grant, M.D., F.R.S. (London); G. H. Newns, M.D. (London); A. H. Imrie, M.D. (Glasgow); G. R. Ellis, M.D. (Liverpool); T. M. Greenaway, M.B. (Australia); K. D. Keele, M.D. (Middlesex); J. H. Kellgren, M.B. (Manchester); S. A. Propert, M.B. (Colchester); W. S. Tegner, B.M. (London); J. E. G. Pearson, D.M. (Bristol); J. W. D. Bull, M.D. (London); C. R. St. Johnston, M.B. (Birmingham); H. J. Wallace, M.D. (London); D. H. Davies, M.B. (Bristol); W. W. Payne, M.B. (Watford); J. W. Crofton, M.D. (London); J. D. Hay, M.D. (Liverpool); J. B. Rennie, M.D. (Glasgow); Sheila P. V. Sherlock, M.B. (London); W. Mayer-Gross, M.D. (Dumfries); C. Wilson, D.M. (London); W. M. Arnott, M.D. (Birmingham); Viscount Addison, M.D., F.R.C.S. (West Wycombe); Sir Alan N. Drury, M.D., F.R.S. (London); Sir Howard W. Florey, M.D., F.R.S. (Oxford); Brigadier J. S. K. Boyd, M.D., F.R.S. (London).

Sir Alun Rowlands was appointed as representative of the College on the Central Council for District Nursing and Dr. P. G. Stock as representative on the Court of the University of Bristol.

Membership

The following candidates, having satisfied the Censors' Board, were elected Members of the College:

Barbara M. Ansell, M.B., A. F. Barnett, M.B., E. T. Bassadone, L.R.C.P., J. H. Baylis, M.B., J. H. Bruce, M.D., W. H. Cary, M.B., F. S. Cooksey, M.D., P. Freedman, M.D., H. R. Gilmore, M.B., H. Greenburgh, M.B., P. G. Griffiths, M.B., F. Grundy, M.D. (*in absentia*), G. W. Hadfield, M.B., S. P. Hall-Smith, M.D., J. P. Horder, B.M., A. W. MacLeod, M.B., C. Pallis, B.M., M. I. M. Pines, M.B., K. Rawnsley, M.B., J. B. Ryder, M.D., J. S. I. Skottowe, M.D., J. M. K. Spalding, B.M., L. Stein, M.B., J. D. Stevens, M.B., K. B. Taylor, B.M., A. W. S. Thevathasan, L.M.S., L. Vogelpoel, M.B., C. A. C. Wiggins, M.B.

Licences

Licences to practise were conferred upon the following 194 candidates (including 30 women) who have passed the Final Examination in Medicine, Surgery, and Midwifery of the Conjoint Board and who have complied with the necessary By-laws:

S. W. Albright, Valerie M. D. Alcock, A. J. Allen, B. Altman, R. A. J. Anthony, G. H. Apthorp, Joyce A. Arscott, J. Ashworth, G. A. E. Baker, Katharine M. Baker, A. A. Bapty, W. R. Barrow, A. P. Barter, P. R. Bateson, Elizabeth L. Batson, T. R. Beatson, T. G. L. Bellis, B. W. Betterton, G. Birch, K. Biss, Pauline M. Bousquet, A. L. C. A. M. Bracchi, A. J. Bridge, A. R. Brighten, N. P. Bronsdon, W. Brumfitt, T. A. Bryant, J. A. B. Burn, Jean M. Burnett, A. M. Burnford, A. C. Campbell, D. S. Carroll, R. D. Catterall, F. A. Chapman, J. S. Clayton, D. J. Cliffe, M. K. Coles, P. H. Connell, B. I. Copeland, Delia M. H. H. Cothay, H. V. W. Coupe, P. H. E. Courtenay, B. P. Courtenay-Mayers, A. N. Cowan, W. H. A. C. Cox, M. J. Craft, K. A. Creamer, Mary D. Daly, Margaret, E. Darling, D. D. Davies, Joan R. Davies, J. P. Davies, D. M. Devane, S. H. Dunce, C. E. Durber, F. P. D. Easby, R. Emery, F. O. Esiri, G. L. Evans, Stella Feldman, A. Ferrari, P. G. Fildes, A. C. Garnham, J.-C. Gazet, Hilda L. Gibbs, M. Gibbs, J. S. Gilbert, A. Gillespie, G. D. Glennie, P. Goodall, J. W. Goodfellow, D. J. C. Graff, Pamela E. Green, D. Greenbaum, J. D. Hackett, M. H. Hambling, T. R. Hamilton, J. W. Hamlett, C. R. Harrison, C. B. L. Hart, P. D. Harvey, M. D. A. Heller, C. B. Higgie, F. E. P. Higgins, B. W. Holbrook, J. B. Holland, D. C. Hood, J. M. Hood, P. T. Hull, Penelope C. Humphries, J. H. M. James, G. H. Jantet, J. C. Jelleyman, G. C. Jenkins, Marion J. P. Jenkins, A. H. John, B. T. Johnstone, G. A. H. Jones, Zilla M. Kaye, R. Keeley, T. D. Kellaway, S. W. Kemp, G. C. E. King, R. H. King, Beryl J. Lander, J. G. Lewis, R. C. Lewis, W. H. J. Llewellyn, A. Ll. Lloyd, C. McKinna, E. J. Masters, W. May, Margaret B. Mearns, J. W. Mercer, P. McK. Middleton, J. L. Montagnon, Ada C. Morrison, F. J. Moynihan, J. W. Murdoch, Shirley E. Nathan, P. J. Nobes, Zofia Nowiak, P. M. J. O'Brien, Mary Ogden, J. O. Ojukwu, J. E. O'Malley, G. P. C. Orlay, D. R. M. P. B. O'Sullivan, J. N. Pachmayr, P. H. Padwick, S. A. C. Paget, J. Palmer, J. A. Parrish, R. E. H. Partridge, J. T. Patton, P. L. Pelmear, Jacqueline S. Pennycuick, R. J. Pett, A. R. Phillips, J. M. Powley, W. J. Pryn, A. Raban-Williams, Mary T. C. Randall, Ann Reader, S. H. Richards, R. A. A. Rickett, J. N. Roper, E. J. Ross, F. L. Rowland, D. L. Rugg-Easey, G. C. Saint, Z. R. Salib, V. Schoengut, D. Scott, Rosamund O. F. Shanks, M. H. Sheard, C. H Sheridan, A. J. Sims, D. P. Q. Smith, R. G. Smith, M. A. Sorefan, K. A. E. Spence, A. G. Spooner, W. J. Stanley, E. H. Stephenson, G. J. Stott, Joan M. M. Sutherland, M. Sutton, J. A. Szydzik, J. Taylor, W. N. A. Taylor, J. Terry, J. L. Tester, Frances M. Thornton, A. W. Tranter, W. M. E. Tweed, V. Udall, J. T. Vorster, D. R. H. Walker, M. A. T. Waters, Monica E. Watkins, M. W. B. Watson, A. N. E. Watt, P. K. B. White, B. R. Wilkinson, W. H. Wilkinson, D. K. Williams, J. F. Williams, R. A. J. Williams, F. Wilson, Vivienne L. L. Wolfson, R. Woodside, E. H. Wyatt, P. A. Zorab.

Diplomas

Diplomas in Child Health were granted jointly with the Royal College of Surgeons of England to G. N. H. Cranswick and to the 77 successful candidates whose names were printed in the report of the meeting of the Royal College of Surgeons of England in the *Journal* of April 28 (p. 961).

Diplomas in Tropical Medicine and Hygiene were granted jointly with the Royal College of Surgeons of England to R. M. Kapadia and to the 34 successful candidates whose names were printed in the report of the meeting of the Royal College of Surgeons of England in the *Journal* of April 28 (p. 961).

Diplomas in Ophthalmology, in Physical Medicine, in Industrial Health, and in Psychological Medicine were granted jointly with the Royal College of Surgeons of England to the successful candidates whose names were printed in the report of the meeting of the Royal College of Surgeons of England in the *Journal* of April 28 (p. 961).

A Diploma in Laryngology and Otology was granted jointly with the Royal College of Surgeons of England to Coroth M. Leelavathi.

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending April 14 (No. 15).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

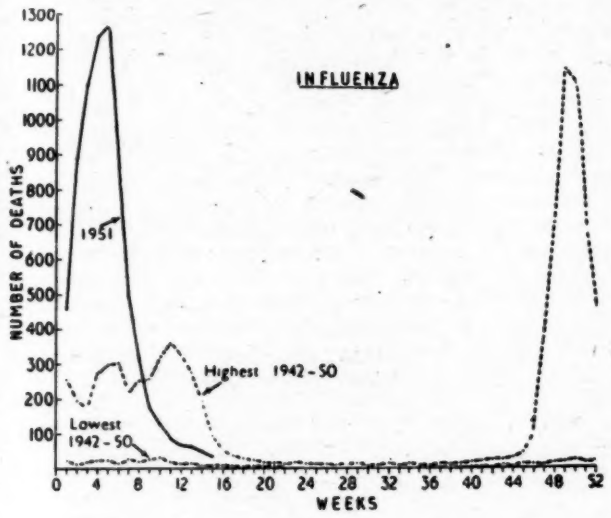
Disease	1951 Week Ending April 14					1950 Corresponding Week					1942–50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	42	7	10	2	2	58	12	19	2	1	783	438	58
Deaths	—	—	—	—	—	—	—	—	—	—			
Dysentery	858	112	147	26	2	303	22	99	1		463	179	49
Deaths		—		—			—						
Encephalitis, acute	13	4	—	—		8	—		—	—	8	2	—
Deaths		—			—		—						
Erysipelas			21	4	9			27	3	6			
Food-poisoning	142	7		1		57	3		—				
Infective enteritis or diarrhoea under 2 years				22	20					16			
Deaths	12		6	2	—	16		3	—	—			
Measles*	22,644	1,610	667	188	131	7,888	171	228	433	95	20,342	9,681	2,552
Deaths		—	1	—	—		—	—	—	1			
Meningococcal infection	46	3	14	1	2	30	4	22	1	1	159	78	27
Deaths		—	2				—	—					
Ophthalmia neonatorum	44	1	11	—		55	—	12	1	2	108	63	44
Pneumonia, influenzal	707	37	4	18	3	722	40	3	15	—	1,150	731	639
Deaths (from influenza)†	33	4	2	1	2	56	5	1	1	6			
Pneumonia, primary			183					173					
Deaths	273	54		14	14	208	35		6	10			
Poliomyelitis, acute:													
Paralytic	15	2	4	—	—	21	1	5	3	4	21	6	4
Non-paralytic	5	—											
Deaths§	—	—			—	1	1			—			
Puerperal fever			3				—	7					
Puerperal pyrexia‖	77	16	3	1	1	85	2	8	2		163	131	81
Scarlet fever	822	52	123	27	67	1,385	100	179	76	96	2,067	1,290	928
Deaths		—	—	—	—			—	—	—			
Smallpox	—	—	—	—		—	—	—	—				
Deaths				—					—				
(1) Tuberculosis, respiratory			169	43				137	31				
(2) Tuberculosis, non-respiratory			28	3				30	6				
(1) Deaths	160	28	28	9	15	199	31	35	7	15			
(2) Deaths		3	1	—	4		2	3	4	3			
Typhoid fever	6	—	1	—	—	5	—	—	1	—			
Deaths¶	—	—	—	—		—	—	—	—		18	9	3
Paratyphoid fever	13	—	4 (B)	1		4	—	2 (A)	—				
Whooping-cough	3,836	272	631	32	84	2,457	110	299	40	86	3,888	1,934	1,234
Deaths	11	—	—	—	—	6	—	—	—	—			
Deaths (0–1 year)	269	51	35	12	21	263	33	25	9	24	554	367	262
Deaths (excluding stillbirths)	5,436	850	632	150	202	5,133	809	618	118	220	5,464	4,706	4,484
Annual death rate (per 1,000 persons living)			12·8					12·4					
Live births	6,948	1,114	908	249	396	7,621	1,224	946	245	467	10,285	7,353	6,262
Annual rate per 1,000 persons living			18·3					19·0					
Stillbirths	182	23	26			205	25	29			256	232	180
Rate per 1,000 total births (including stillborn)			28					30					

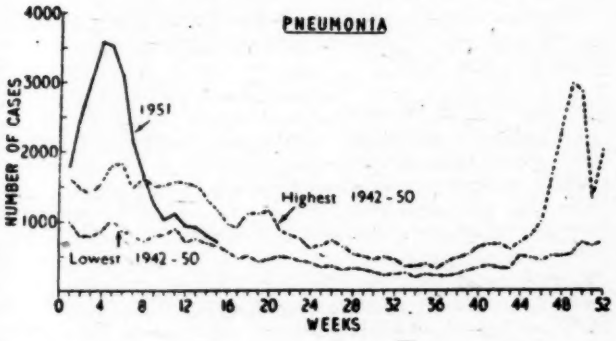
* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

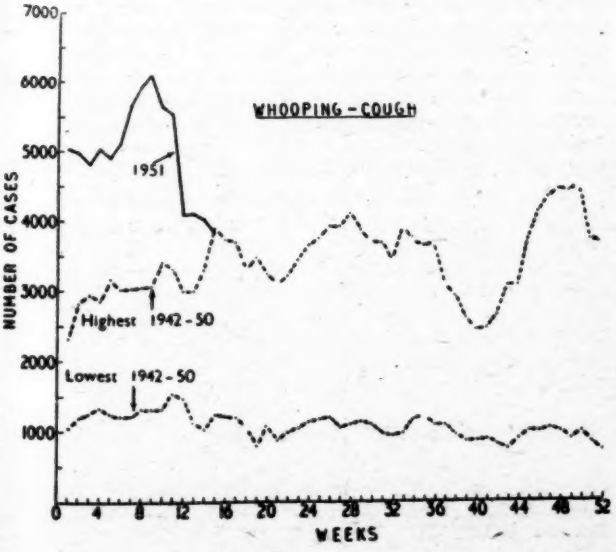
Vital Statistics

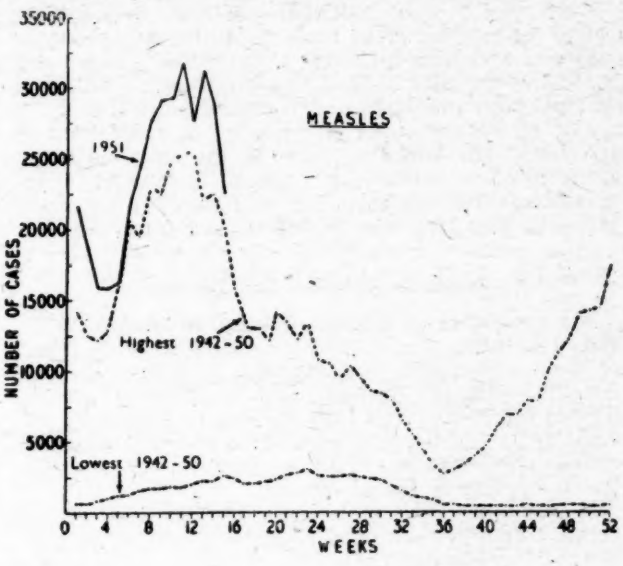
Graphs of Infectious Diseases

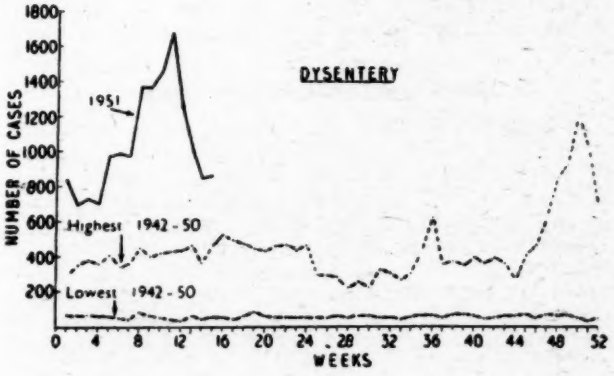
The graphs below show the uncorrected numbers of cases (deaths from influenza) of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus - - - - - -, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.

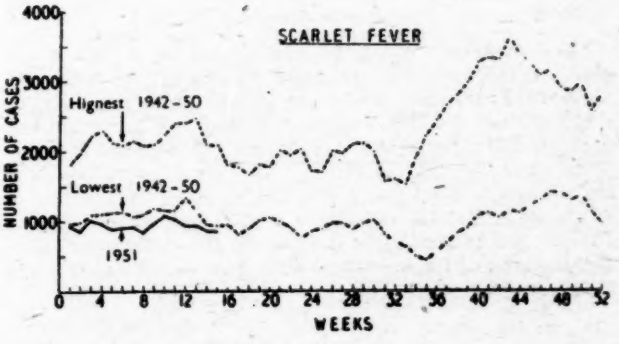












Infectious Diseases

In England and Wales the chief fluctuations in the trends of infectious diseases during the week ending April 14 were decreases in the number of notifications of measles 6,156, whooping-cough 173, and acute pneumonia 92.

A large fall in the incidence of measles was reported from most areas of the country. The largest declines were Yorkshire West Riding 826, Essex 654, Surrey 527, Kent 494, Middlesex 489, London 473, while the chief exceptions to a declining incidence were Cornwall and Yorkshire North Riding with rises of 91 and 80 respectively. No change of any size occurred in the local trends of scarlet fever. The largest falls in the number of notifications of whooping-cough were Yorkshire West Riding 64 and Surrey 73. The notifications of diphtheria were six fewer than in the previous week, the chief feature of the returns being a fall of 4 in Warwickshire. In Scotland the notifications of diphtheria were 13 fewer than in the preceding week.

There were 5 more notifications of acute poliomyelitis than in the previous week; the areas with multiple notifications were Middlesex 3, London 2, Derbyshire 2, Lancashire 2. Seventy-six cases of food-poisoning were notified from the rural district of Whitby in Yorkshire North Riding. A rise of 12 was reported in the number of notifications of dysentery. The largest variation in the local returns of dysentery was a fall of 75 in London. The largest returns were Lancashire 116, London 112, Middlesex 105 (Edmonton M.B. 61), Yorkshire West Riding 62, and Surrey 60.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in March was 128, compared with 147 (revised figure) in February and 129 (revised figure) in March, 1950 (*Ministry of Labour Gazette*, April, 1951). Of these, 24 were deaths underground in coal mines. There were also 27 deaths of seamen—23 on trading vessels and four on fishing vessels.

The following cases of industrial diseases were reported during March in the United Kingdom: lead-poisoning, 2; mercurial poisoning, 1; aniline poisoning, 1; epitheliomatous ulceration, 8; chrome ulceration, 26 (chromium plating, 21). There were no cases of anthrax and no deaths.

Births and Deaths in First Quarter

In England and Wales the birth rate during the quarter was 16.3 per 1,000 total population; this rate was 0.4 below the rate for the March quarter of 1950. The stillbirth rate was 23.6 per 1,000 total births and was 0.7 above the rate for the previous first quarter. Infant mortality was 38.2 per 1,000 related live births, being 1.4 above the rate for the March quarter of 1950. The general death rate was 19.0 per 1,000 total population—5.0 above the rate for the corresponding quarter of 1950. With the exception of a rate of 19.9 in the first quarter of 1940 this was the highest death rate for any quarter for 25 years.

Indian Census

The population of India, enumerated in a census on March 1, is 356,891,624. Of these, 183,384,807 are males and 173,506,817 are females. The census excluded Jammu, Kashmir, and the tribal areas of Assam. When estimated populations for these areas are included, the increase in population since the previous census of 1941 is 42.06 million over the previous official figure of 1948–9. India's population is 15.1% of the world population and comes second only to China's, whose population is 19.4% of the world population. But the area of China is more than three times that of India (*India News*, April 21, 1951).

Week Ending April 21

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 948, whooping-cough 3,498, diphtheria 32, measles 19,025, acute pneumonia 551, acute poliomyelitis 22, dysentery 1,002, paratyphoid fever 12, typhoid fever 4. Deaths from influenza in the great towns numbered 16.

The British Council recently organized a course on port health in London and Liverpool. Visitors from the Netherlands, Belgium, Italy, France, Portugal, and British Guiana, including the port health inspector from Antwerp, the medical officer of Lisbon port, and other public health officials, studied the fumigation of ships, ways of dealing with rodents in docks and vessels, and systems of examining imported foodstuffs. A week was spent in London inspecting the docks, hospitals, and warehouses, and then the course transferred to Liverpool for a further week's programme.

Medical News

Care of Cripples

Mr. Hilary Marquand addressed the annual meeting of the Central Council for the Care of Cripples held in London on April 20. He said that all concerned with the treatment and rehabilitation of the disabled must have been pleased that, since the beginning of the National Health Service, services previously available only to special groups, such as the war-disabled, had become universally available. The Ministry of Pensions had an excellent production and supplies division, and the experience gained in obtaining various appliances for the war pensioner had now been turned to the advantage of the civilian. For every artificial limb supplied to-day to war pensioners two were supplied to civilians under the National Health Service. In all, since the start of the Service, 15,060 tricycles and chairs had been supplied to Health Service patients up to March 16, 1951. This meant that the disabled were afforded not only immense joy and satisfaction but also were enabled to go to work, and that was essential for successful rehabilitation. There was close co-operation in preparing a directive to local authorities on their tasks under the National Assistance Act. Informal conversations were taking place between the Ministry, local authorities, and other organizations concerned with the disabled, and when the directive was issued it would be an agreed document. The Minister hoped that local authorities would study it carefully and be determined to play their part in the construction of a really adequate service for the handicapped citizens of the country. Though that might cost money it would, in the long run, be of economic as well as social benefit. It would be money invested in rehabilitating those who would otherwise be unable to contribute to the productive effort so vital to the welfare of the nation as a whole. There was need also—and this was where the Minister paid a special tribute to the value of the work being done by the Central Council for the Care of Cripples—to develop the training given to workers in this field.

Kingston Victoria Hospital

The Ministry of Health announced on April 27 that it could see no justification for further delay in converting the hospital to meet the gynaecological needs of the area. All alternative proposals put forward are said to be unworkable, and the Minister has now authorized the regional board to convert the hospital. It will close on May 31, and no admissions may be made after May 7. It is understood that invitations have been sent to every general practitioner in the Kingston Group—numbering about 140—to join the staff of what was formerly known as the Surbiton Annexe, now the Claremont Hospital, where there are 26 beds. Dr. T. W. Morgan states that the whole affair is a gross breach of faith; the Claremont Hospital is not even to be administered by its own house committee; the intention appears to be utterly to destroy the identity of the Victoria Hospital.

Seminar on World Health Organization

During the World Health Assembly at Geneva (May 7–18) a seminar will be held for those young doctors and medical students who are interested in the world-wide aspects of social medicine. One or two conferences will be held every day, covering world medical co-ordination, organization of public hygiene, promotion of health, and so on. All the meetings will take place at the Palais des Nations, and further information may be obtained from the secretariat, Villa Rigot, 1, Avenue de la Paix, Geneva.

National Association for the Paralysed

The address of the National Association for the Paralysed, formerly 1, Dorset Buildings, Salisbury Square, London, E.C.4, is now Tavistock House (South), Tavistock Square, London, W.C.1 (Tel.: Euston 2392).

Price's "Medicine"

A dinner was held on April 17 at the Athenaeum on the occasion of the publication of the eighth edition of *A Textbook of the Practice of Medicine*. Dr. F. W. Price was the guest of honour. Mr. Geoffrey Cumberlege, publisher to the University of Oxford, was the host, and in a short speech expressed regret that Dr. Price was retiring from the editorship of the book, and announced that his successor would be Dr. Donald Hunter. He recalled the history of the *Textbook*, which was first published in 1922, and noted that the sales were now divided almost exactly equally between Great Britain and overseas.

North of England Obstetrical and Gynaecological Society

A meeting was held in Sheffield on March 30, when Mr. S. Bender (Liverpool) described a case of persistent discharge after vaginal hysterectomy, eventually found due to a carcinoma of the Fallopian tube. Dr. C. G. Paine (Sheffield) reported a case of Pick's adenoma of the ovary, and Mr. L. B. Patrick (Sheffield) presented a case of a masculinizing adrenal tumour. Dr. A. A. Smith (Leeds) described a clinical aid to the assessment of cephalo-pelvic disproportion in the last weeks of pregnancy, by rectal examination of the patient standing erect.

£50 Award

The committee of the Oliver Memorial Fund is to make the fourth award of £50 to a British subject whose services in connexion with blood transfusion are considered to be a notable contribution to the research, organization, or donor aspect of this subject. Applications will be welcomed (before June 30), and also information about suitable candidates. All correspondence should be addressed to the honorary treasurer, F. W. Mills, Esq., c/o National Provincial Bank, Ltd., Holborn Circus, E.C.1.

Central Index of Translations

The Association of Special Libraries and Information Bureaux is preparing a central index of translations, including scientific papers, reports, and published articles which appear in foreign journals. All help and inquiries should be addressed to ASLIB, 4, Palace Gate, London, W.8.

Nurses' Health

King Edward's Hospital Fund for London has issued a revised memorandum on the *Supervision of Nurses' Health* (3d., post free, from the Fund) with the warm approval of the Minister of Health. It recommends that there should be a physician specially for the nursing staff, and proposes that on entering hospital a nurse should have a thorough compulsory medical examination, chest *x*-ray examination, vaccination against smallpox, and diphtheria immunization. Accommodation for sick leave is discussed, and no nurse should be allowed to return to duty until passed by the physician. Active preventive measures against tuberculosis infection are outlined, including compulsory three-monthly *x*-ray examination.

Publications Received

Architects' Co-operative Partnership: *A New Hospital for St. Albans: Report* (1950). The International Hospital Federation: *Report of the Study Tour of Hospitals in Sweden* (September, 1950). Ministry of Fuel and Power: *Accident at Knockshinnoch Castle Colliery, Ayrshire* (H.M.S.O., 2s. 6d.). The National Corporation for the Care of Old People: *Third Annual Report* (1950). The Pharmaceutical Society of Great Britain: *Registrar's Report for 1950*. The Tavistock Clinic: *Report for the Year 1949*. Order of St. John and the British Red Cross Society: *Fifth Report of the Joint Committee. Gas in the Public Health Services.*

In Brief

Dr. Fritz Linder, chief resident surgeon at Heidelberg University Hospital, specialist in vascular diseases and thoracic surgery, recently spent two weeks in Britain studying recent advances in British surgery.

At the meeting of the Central Midwives Board held on April 5 Mr. Arnold Walker was re-elected as chairman and Mr. J. P. Hedley as vice-chairman for the ensuing year.

Mr. H. J. Seddon, Director of Studies at the Institute of Orthopaedics, Royal National Orthopaedic Hospital, London, is lecturing at Stockholm, Lund, Upsala, and Oslo during May.

Wills

Dr. Daniel Charles Edington, of Penrith, Cumberland, left £25,024. Dr. William Alexander Kirkpatrick, for some years in general practice at Skelton-in-Cleveland, in the North Riding of Yorkshire, left £18,837. Dr. Gilbert William Charsley, formerly in practice in Sydenham, a former chairman of the Lewisham Division of the B.M.A., left £7,133. Dr. Stephen Roodhouse Gloyne, respiratory pathologist, and a recognized authority on industrial diseases of the lung, consulting pathologist to the London Chest Hospital, and King Edward VII Sanatorium, Midhurst, Sussex, president of the British Tuberculosis Association in 1938, and vice-president of the Thoracic Society at the time of its formation, left £2,210. Dr. Charles Edward Boyce, a Dublin anaesthetist, left estate valued at £54,215. He left £1,000 to the Grand Benevolence of the Order of the Friendly Brothers of St. Patrick, St. Stephens Green, Dublin, for the benefit of the order, and various personal bequests.

Lieutenant-Colonel Geoffrey Percy Humphery, of Stradbroke, Suffolk, left £6,561. Dr. Alexander Thomas Harrison, of County Durham, left £11,345. Lieutenant-Colonel William Glen Liston, of Morar, Inverness-shire, formerly bacteriologist, Royal College of Physicians, Edinburgh, left £25,298. Surgeon Commander Drummond Rewcastle Forbes Bertram, of Ilminster, Somerset, left £6,055. Dr. Francis Christopher Plummer, of Wirral, Cheshire, left £47,634. Dr. George Bertram Wainwright, of Cirencester, Glos, at one time senior physician at the Royal Hampshire County Hospital, and for many years medical officer to Winchester College, left £37,881; he requested that "no more than is necessary for decency be spent on my funeral." Mr. Martin Witham Palmer, of Surbiton, left £236,082; among other bequests he left £50 to Mr. Stevens, "The taxicab driver I employ," and the residue between the Distressed Gentlefolks Aid Association, St. Dunstan's, Dr. Barnardo's Homes, Royal Association in Aid of the Deaf and Dumb, R.N.L.I., King George's Fund for Sailors, and the British Empire Cancer Campaign.

Dr. Cyril Mary Brophy, of Wimbledon, left £10,162. Dr. Robert Fielding-Ould, consulting physician, Mount Vernon Hospital for Diseases of the Chest and to the Ministry of Pensions, who had travelled extensively in the Far East on leprosy and malaria research missions and was also a barrister-at-law of the Inner Temple, left £354. Dr. Andrew Fleming Galloway, of Sidmouth, Devon, left £17,625, including bequests to the University of Glasgow, to encourage research work on diseases of children, and to the Royal Hospital for Sick Children, Glasgow, to endow cots in the surgical ward. Dr. Charles Claud Twort, of Sussex, left £15,668. Dr. Saville James Fielding, former resident medical superintendent of the Bethel Hospital, Norwich, left £11,934.

Dr. Oliver Edward McCutcheon, for over 30 years in practice in India, left £6,346. Dr. Herbert Anderson Eccles, of County Durham, a former Durham County rugby footballer, left £11,000. Dr. David Blair, of Edinburgh, formerly medical superintendent, County Mental Hospital, Prestwich, Lancs, and lecturer in mental diseases, University of Manchester, left £39,299. Dr. Henry Bret Russell, of Ashford, Kent, for many years in charge of the electrocardiographic department at St. Thomas's Hospital, left £12,471.

Dr. William James Walters, late of Swansea, left £13,410. Dr. Thomas Clifford, of Stalybridge, Cheshire, left £17,093. Dr. Francis James Strong Heaney, formerly of Southport, president of the Lancashire and Cheshire Branch of the B.M.A., 1923–4, and chairman of the Liverpool Division, 1926–7, left £14,064. Mr. William Fry, late of the Colonial Service, left £66,154; after various bequests the residue to be divided equally between the Boy Scouts Association, the Shaftesbury Homes and *Arethusa* Training Ship, the Royal Medical Benevolent Fund, the Royal United Kingdom Beneficent Association, the National Benevolent Institution, the British Home and Hospital for Incurables, Streatham, the Distressed Gentlefolks Aid Association, the Royal National Pension Fund for Nurses, the Fairbridge Farm Schools, Lloyds Patriotric Fund, the National Society for Promoting Religious Education, and the Church Army. Dr. Donald Alexander Fraser, of Inverness, left £11,008. Dr. Robert Horsburgh Tait, of Edinburgh, left £7,892. Dr. Andrew Elliot, of Fleet, Hants, left £33,895; among other bequests 10 guineas to the qualified medical man who severed a main artery in his body after his death, and a residue to be divided between Dr. Barnardo's Homes, Quarriers Homes, and the Church of Scotland's Social Service Homes for the Aged. Dr. Herbert Bree Emerson, of Pershore, Worcs, left £23,342. Dr. Douglas Martin Spring, of West Bromwich, Staffs, left estate, "so far as at present can be ascertained," valued at £18,024.

COMING EVENTS

Institute of Dermatology

A course of lectures is being given, lasting until June 22, and also a special series of clinical demonstrations at 5 p.m. on Fridays for postgraduates studying for the M.R.C.P. and other diplomas. Inquiries should be addressed to the Institute of Dermatology, St. John's Hospital for Diseases of the Skin, Lisle Street, W.C.2.

Chemistry in the Service of Man

Four popular lectures under this general title on the conquest of disease, food, the amenities of life, and modern thought have been arranged by the Chemical Council, and will be given at the Royal Institution, 21, Albemarle Street, W.1, on May 16 and 23 at 3 p.m. and on May 30 and June 6 at 6 p.m. Admission will be free by ticket, and all information is available from the Ticket Secretary (Lectures), the Chemical Council, 9–10, Savile Row, W.1.

Course on Photomicrography

Six lectures on photomicrography, including its practice in medical science and the use of phase-contrast techniques, will be given by Mr. Harold Malies at the London School of Printing and Graphic Arts, Bolt Court, Fleet Street, E.C.4, on Monday evenings at 6 p.m., commencing May 21. As space is limited, early application should be made in writing to the secretary at the school. The fee for the course is 10s.

History of Pharmacy

Sir Howard Florey, F.R.S., will open an exhibition prepared by the Wellcome Historical Medical Museum illustrating the history of pharmacy at the Wellcome Research Institution, 183–193, Euston Road, London, N.W., on Tuesday, May 8, at 3.30 p.m.

Montessori Society

The Ninth International Montessori Congress will be held at the Royal Institution from May 11 to 19 (including Whitsun). The subject of the congress, at which the president and principal speaker will be Dr. Maria Montessori, is "Education as an Aid to the Natural Development of the Psyche of the Child from Birth to University." The syllabus and full details may be obtained from the secretary, Mrs. P. Wallbank, Montessori Society, 14, Gordon Square, W.C.1.

Hospital Administration

The annual conference of the Institute of Hospital Administrators will be held at Eastbourne, May 17–19. Papers will be read on problems of both central and local hospital administration, and there will be a discussion of the needs of the hospital service. The programme and all details may be obtained from the secretary, Institute of Hospital Administrators, 75, Portland Place, London, W.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday

EDINBURGH UNIVERSITY.—At Physiology Class Room, May 7, 5 p.m., "*The Hippocratic Ideal*," by Dr. Douglas Guthrie.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—May 7, 5.30 p.m., "*Sympathetic Ophthalmitis*," by Mr. M. H. Whiting.

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, London, W.—May 7, 8.30 p.m., general meeting; 8.45 p.m., "*Migrainous Variants*," Annual Oration by Sir Charles Symonds.

UNIVERSITY COLLEGE.—At Anatomy Theatre, Gower Street, London, W.C., May 7, 5.30 p.m., "*On the Comparative Study of Behaviour*," Inaugural Lecture by Dr. R. W. Russell.

UNIVERSITY COLLEGE.—At Chemistry Lecture Theatre, Gower Street, London, W.C., May 7, 5.30 p.m., "*Recent Advances in the Chemistry of Natural Products*," last of three Special University Lectures by Professor R. B. Woodward, Ph.D. (Harvard University).

Tuesday

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 41, Queensgate Terrace, London, S.W., May 8, 7 for 7.30 p.m., annual dinner.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 8, 5 p.m., "*Tuberculosis of the Skin*," by Dr. G. B. Dowling.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—May 8, 5 p.m., "*Professional Freedom*," Croonian Lecture by Dr. T. Fortescue Fox.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—May 8, 5 p.m., "*Non-paralytic Strabismus*," by Dr. T. H. Whittington.

ST. MARY'S HOSPITAL MEDICAL SCHOOL: WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, Paddington, London, W.—May 8, 5 p.m., "*Antigen and Antibody*," Almroth Wright Lecture by Professor H. R. Dean.

Wednesday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 9, 5 p.m., "*Cellulae Naevi and Melanomas*," by Dr. H. Haber.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—May 9, 5.30 p.m., "*Recent Advances in Ocular Therapeutics*," by Mr. H. Ridley.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—May 9, 2.30 p.m., visit to Queen Elizabeth's Training College for the Disabled, Leatherhead, Surrey.

SOCIETY OF CHEMICAL INDUSTRY: FOOD GROUP.—At Burlington House, Piccadilly, London, W., May 9, meeting of Nutrition Panel. (1) 6 p.m., annual general meeting; (2) 6.15 p.m., scientific meeting. "*Antibiotics in Nutrition*," by Dr. W. F. J. Cuthbertson.

Thursday

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, London, W., May 10, 8 p.m., "*The Neurotic Life-style*," by Dr. A. R. Redfern. Discussion to be opened by Dr. Donald Blair.

DUBLIN UNIVERSITY, Trinity College Dublin.—At Physiology Theatre, May 9, 4.30 p.m., "*The Importance of Noradrenaline*," John Mallet Purser Lecture by Professor J. Harold Burn, F.R.S.

EDINBURGH UNIVERSITY, University New Buildings (Anatomy Theatre), Teviot Place, Edinburgh.—May 10, 5 p.m., "*Injuries of the Female Bladder and Urethra*," Honyman Gillespie Lecture by Professor C. Scott Russell.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 10, 5 p.m., "*Cutaneous Manifestations of the Reticuloses*," by Dr. B. Russell.

OXFORD UNIVERSITY.—At Nuffield Department of Orthopaedic Surgery, Oxford, May 10, 8.30 p.m., "*Fundamentals Related to Surgical Procedures in Orthopaedic Surgery*," by Professor E. Harlan Wilson (Columbus University, U.S.A.).

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—May 10, 3 p.m., "*Exophthalmos*," ophthalmology lecture by Mr. J. H. Mulvany; 5 p.m., "*Constrictive Pericarditis*," surgery lecture by Professor Emile Holman.

ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, May 10, 5 p.m., "*A Realistic Approach to the Problem of Anaemia*," by Sir Lionel Whitby.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—May 10, 4.30 p.m., "*Neurology*," lecture-demonstration by Dr. Denis Williams.

UNIVERSITY COLLEGE.—May 10 (1) At Chemistry Theatre, Gower Place, London, W.C., 4.45 p.m., "*Energy Transformations in Living Matter*," by Professor H. A. Krebs; (2) At Physiology Theatre, Gower Street, London, W.C., 5.15 p.m., "*Studies on the Regulation of Arterial Blood Pressure*," by Professor G. Liljestrand (Stockholm).

WYE COLLEGE, Swanley Hall, near Ashford, Kent.—May 10, 8 p.m., "*Monkeys and Agriculture*," by Professor S. Zuckerman.

Friday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 11, 5 p.m., lecture-demonstration.

APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Medical Registrar at United Norwich Hospitals*, S. D. Stock, M.B., B.S., F.R.C.S.Ed. *Surgical Registrar at Great Yarmouth and Gorleston Hospital*, J. B. Binks, M.B., Ch.B.

MITCHELL, JOHN BERNARD, M.D., M.R.C.P., Consultant Physician, Bolton and District Hospital Group; Consultant Chest Physician, Bolton Chest Clinic and Group Hospitals having Tuberculosis Beds.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—*Senior Hospital Medical Officer Anaesthetist to North Gloucestershire Clinical Area*, J. E. Tees, M.R.C.S., L.R.C.P., D.A. *Consultant Physician in Psychiatry with Special Knowledge of Electroencephalography to Bristol Mental Hospitals*, E. C. Turton, M.Sc., M.B., B.S., M.R.C.P., D.P.M. *Anaesthetic Registrars to Frenchay Hospital, Bristol*, Pamela Westhead, M.B., Ch.B., D.A., and R. D. Levis, M.B., B.Ch., D.A.

THOMPSON, CYRIL GEORGE KAY, M.B., Ch.B., D.P.H., Medical Officer of Health, Wakefield County Borough Council, Yorks.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Allen.—On April 27, 1951, at Colchester Private Nursing Home, to Judy, wife of Dr. Richard Allen, of Castle Hedingham, Essex, a daughter.

Bailey.—On April 19, 1951, at University College Hospital, London, W.C.1, to Jeanne, wife of David Bailey, F.R.C.S., a son—David Michael.

MARRIAGES

Manson—Chaloner.—On April 28, 1951, at Salisbury, Southern Rhodesia, John M. S. Manson, M.D., D.T.M.&H., D.R.C.O.G., of Arbroath, Scotland, and Molepolole, Bechuanaland Protectorate, to A. Jocelyn C. Chaloner, M.S.T., C.T., of Salisbury.

DEATHS

Abbott.—On April 26, 1951, at St. George's Hospital, Samuel Herbert Lee Abbott, D.S.O., M.B., Lieutenant-Colonel, I.M.S., retired, aged 73.

Brewis.—On April 23, 1951, at 8, Esplanade Crescent, Scarborough, Edward James Brewis, M.D., late of Willington, Co. Durham.

Burton.—On April 26, 1951, at Shanghai, Thomas Menzies Burton, M.B., Ch.B.

Culross.—On April 21, 1951, James Culross, M.B.E., M.B., C.M., of 9, Courtenay Park, Newton Abbot, Devon.

De Gébert.—On March 8, 1951, Louis Jean Adam de Gébert, M.R.C.S., L.R.C.P., of 3, Clarence Road, Herne Bay, Kent, formerly of Hornsey, London, N.

Edwards.—On April 20, 1951, at Berwyn, Heathside Close, Northwood, Middlesex, David Glyn Mason Edwards, M.B., B.S., D.P.H.

Edwards.—On April 29, 1951, at Harrogate, Francis Henry Edwards, M.B., F.R.C.S.Ed., of 14, St. John's Hill, Shrewsbury.

Elliott.—On April 13, 1951, the result of an accident, Kenneth Alwyne Elliott, M.R.C.S., L.R.C.P., of Albrighton, near Wolverhampton, Staffs, aged 29.

Little.—On April 24, 1951, at West London Hospital, Andrew Hunter Little, M.R.C.S., L.R.C.P., of 4, Wellesley Road, Chiswick, London, W.

McCann.—On April 23, 1951, at Cambridge Military Hospital, Aldershot, Henry James McCann, M.B., B.Ch., Major, R.A.M.C.

Porter.—On April 25, 1951, at Princess Alice Hospital, Eastbourne, William Ernest Porter, M.D., D.P.H., J.P., of "Woodeen," Decoy Drive, Hampden Park, Eastbourne, aged 88.

Powell.—On April 27, 1951, at Sudbury, Suffolk, Rhys Vaughan Powell, F.R.C.S., aged 60.

Speechly.—On April 26, 1951, at Overcliff, Teignmouth, Alec John Lincoln Speechly, M.R.C.S., L.R.C.P., late of Leicester.

Tennent.—On April 26, 1951, at Nakuru, Kenya, James Hall Tennent, M.B., F.R.C.S.Ed.

Towlson.—On April 24, 1951, at his home, "Homewood," Charlton, near Andover, Hants, Henry Joseph Towlson, M.R.C.S., aged 94.

Verrall.—On April 22, 1951, at St. John and St. Elizabeth Hospital, Paul Jenner Verrall, M.B., F.R.C.S., of 48, Carlton Hill, St. John's Wood, London, N.W., aged 68.

Wallace.—On April 26, 1951, at his home, Belgrave House, Palace Road, East Molesey, Surrey, George Smith Wallace, O.B.E., M.B., Ch.B., D.P.H., Colonel, late R.A.M.C., retired, aged 72.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Paratyphoid Carriers

Q.—*(1) What is the best treatment for a paratyphoid carrier? (2) What criteria of cure should be adopted? (3) How can journals, textbooks, etc., be disinfected after use by a carrier?*

A.—(1) If paratyphoid bacilli or any organisms of the enteric group persist in the faeces after recovery from the disease, it is worth waiting for several months, in the hope that they will disappear spontaneously, before adopting any drastic measures. A sample of bile should then be obtained by duodenal intubation in order to verify that the gall-bladder is infected, as is usually the case. Cholecystectomy has then to be considered: this removes the main focus of actual infection, and sometimes achieves a radical cure. Of various forms of chemotherapy which have recently been tried, none has had any consistent success, although the bowel can usually be temporarily cleared of detectable bacilli by large doses of succinylsulphathiazole, streptomycin given by the mouth, or both drugs together. Such treatment may reasonably be given after cholecystectomy to help to eliminate bacilli remaining in the bowel. It is well established that chloramphenicol, although a specific for the disease itself, is useless for treating the carrier state.

(2) The criterion of cure is a series of negative stool cultures in selective media: to establish the cure of a persistent carrier at least six such cultures should be made over a period of several months.

(3) The known carrier should avoid contaminating books and other objects by scrupulous cleanliness in defaecation and thorough subsequent washing and disinfection of the hands. The disinfection of books, if necessary, is best carried out with formaldehyde vapour.

Tics

Q.—*What is known about the aetiology and treatment of tics?*

A.—There is still something mysterious about tics or "habit spasms." There seems to be no doubt that psychological factors are important in their aetiology, and many consider tics to be frankly hysterical. This is not, however, the whole story, for the repetition of one movement in certain delicately balanced muscle groups (e.g., of face or neck) seems to lead to the establishment of such a strong neuronal pattern that what began as a habit gradually becomes a physiological function tending to persist on and off throughout life. The occurrence of the well-established habit spasm is largely conditioned by the degree of emotional tension at the time, and the movement often ceases during physical and mental relaxation.

With regard to treatment, the habit spasms of children generally cease as age advances, but when severe spasms persist into adult life or develop later in life (as with spasmodic torticollis) then there is little prospect of any permanent cure. It is, of course, important that the patient should realize that a habit spasm is not a condition which leads to organic disease. "An irritation which does not matter much" is a healthy attitude, as the patient at heart worries a lot and is self-conscious about the spasm. General sedatives should seldom be continued for long, but an attempt should be made to reorganize the patient's life in such a way as to reduce situations leading to mental tension and anxiety. In this connexion a short period of complete rest in bed, away from home and relations, is often helpful.

The patient's personal attitude to the disability often requires correction. In some cases it is helpful to introduce some physical means to resist the muscle spasm. For example, a plaster collar may give relief to cases of spasmodic torticollis. Muscle-relaxing drugs are not of much value in this type of case.

Contraindications to Methonium Salts

Q.—*Are methonium compounds advised in cases of hypertension (a) complicated by advanced arteriosclerosis, or (b) after a cerebral vascular accident has occurred?*

A.—Methonium compounds may be dangerous in both these conditions, and also in a third group—namely, in hypertensive patients in whom angina pectoris is attributed more to coronary atherosclerosis than to the increased cardiac work resulting from hypertension. In all these conditions marked lowering of the blood pressure may have disastrous consequences. If the survival of an area of cardiac muscle is critical, necrosis may well follow sudden drastic lowering of the blood pressure whether there is secondary coronary thrombosis or not.

Recently, a hypertensive patient was seen who had bouts of slight weakness of the left side of the face and left hand which were attributed by her doctor to cerebral vascular spasm. Although there was very little to find, it seemed more likely that the blood supply to the appropriate part of her brain was critical, and that the methonium compounds, far from relieving cerebral vascular spasm, might precipitate a stroke when the pressure fell. Nevertheless, as her doctor had observed her in many attacks, his view could not be lightly dismissed, and it was therefore agreed to try methonium under controlled conditions, and to abandon the drug if the symptoms were worse as the pressure fell. This is precisely what happened, and the drug was at once abandoned. Although this patient did not seem any worse two days later, when the blood pressure had regained its previous level, she developed a left hemiplegia from cerebral thrombosis shortly afterwards.

Coeliac Disease and Hexamethonium Salts

Q.—*I have read in the "Journal" (1951, 1, 552) of hexamethonium bromide being successfully used in steatorrhoea following gastrectomy. Has it been tried in coeliac disease? If so, with what result, and in what dosage?*

A.—The steatorrhoea following gastrectomy appears to be largely due to incoordination and small-intestinal hurry. Both the absorptive capacity of the upper small intestine and the jejunal radiographic pattern are usually normal. Hexamethonium bromide slows the intestinal movements, so that absorption is improved.

The steatorrhoea of the sprue syndrome, of which coeliac disease is an example, is due to interference with the particulate absorption of glycerides. There is small-intestinal delay in most cases; the absorptive capacity of the small intestine, not only for fats, but also for glucose, urea, and other substances, is depressed; the radiographic flocculation pattern is observed, indicating excessive secretion of mucus. There is therefore little indication for the use of hexamethonium bromide in coeliac disease or other forms of the sprue syndrome, and no reports of its use have so far been published.

Frying-oils

Q.—*Does the frying of foods in (a) mineral oils and (b) vegetable oils have any ill effect on the health?*

A.—This question involves two different problems. First, the desirability or otherwise of the use of the normal raw oils in foods, and, secondly, whether the heating of the oils, perhaps repeatedly, may bring about changes affecting their action in man.

For many years there has been evidence of absorption of mineral oils (see *British Medical Journal*, 1950, 1, 857). Since the metabolic implications of the assimilation of these substances are unknown it is generally agreed that their inclusion in foods is undesirable. Although well-fried foods should carry little of the frying-oil with them, this cannot be guaranteed, and the use of mineral oil for frying is therefore to be deprecated. The heating of mineral oils may give rise to changes in the oil which might add further risks to their ingestion by human subjects.

The use of uncooked vegetable oils in food has not been shown to have any deleterious effects on health. If unsaturated oils are used, and especially if they are repeatedly heated and cooled, oxidative rancidity may occur. The products of rancidity may cause severe changes in gastrointestinal function. There is some evidence to suggest that rancid fats may be one of the aetiological factors in tropical sprue.

Skin Tests for Syphilis

Q.—*What is the "luotest" reaction? How is it performed, and how reliable is it?*

A.—This is a modification of the luetin intradermal test, once used, but now discarded, in the diagnosis of syphilis, both tests being similar in principle to the cutaneous tuberculin test. Extracts either of syphilitic organs or killed ascites-agar cultures of *T. pallidum* (Noguchi) are employed for the luetin reaction, whereas for the modification we are considering the extract, marketed in Vienna under the name of luotest, is made from acute syphilomas of rabbits' testicles. The test is performed by injecting 0.2 ml. of luotest and the same quantity of control solution into the flexor surface of the forearm: the result is read 24 and 48 hours later. A positive reaction shows a well-defined erythematous patch 10 mm. or more in diameter. In some cases a red papule (occasionally necrotic) appears in the patch. Positive reactions, most frequent during the latent and tertiary stages of the disease, are rarely obtained during the primary and secondary phases. Both luetin and luotest have been proved to be non-specific and are not recommended for the diagnosis of syphilis at any stage.

Enlargement of the Thyroid

Q.—*A woman of 32 has had a slight swelling of the left lobe of the thyroid for the past nine years. During the last few months it seems to have been enlarging slightly. There are no symptoms of hypo- or hyper-thyroidism. Would you advise iodine? If so, for how long, and in what dosage? What are the prospects of the swelling subsiding?*

A.—There is no reason to suppose that administration of iodine will affect the swelling of this patient's thyroid gland. It is probably part of a non-toxic nodular goitre, but other possibilities exist, and the risk of carcinoma must not be forgotten. It is most unlikely to subside spontaneously after having been present for nine years. It would be advisable to seek a surgical opinion, particularly if progressive enlargement continues.

Liver Extracts in Banti's Syndrome

Q.—*Are liver extracts of value in the treatment of Banti's syndrome?*

A.—The term Banti's syndrome is most commonly used to mean chronic congestive splenomegaly; the syndrome is therefore no more than a symptom of obstruction to the portal circulation. In this sense, liver extract could be of no possible value in treatment. If, however, the term is applied to some form of hepatic cirrhosis, which is the common pathological process underlying portal obstruction, it is conceivable that liver extract might be of some therapeutic benefit.

FESTIVAL SCIENTIFIC MEETINGS

Summary of Symposia

JUNE

Date and Time	*Subject*	*Convener or Chairman*
Mon., 4; 2.00 ..	The Peripheral Nervous System	Sir Henry Dale
Tues., 5 ..	—	—
Wed., 6; 10.30 and 2.30	Otorhinolaryngology ..	Mr. W. M. Mollison
Thurs., 7; 2.15 ..	Antibiotics	Sir Alexander Fleming
Fri., 8; 4.00 ..	Vascular System (Clinical)	—
Mon., 11; 2.30	Ophthalmology	—
Tues., 12; 10.30	Plastic Surgery	Sir Gordon Gordon-Taylor
2.00	Plastic Surgery (cont.) ..	Sir James Paterson Ross
Wed., 13 ..	—	—
Thurs., 14; 2.00	Central Nervous System ..	Dr. W. Russell Brain
Fri., 15; 4.30 ..	Anaesthetics	Dr. I. W. Magill
Mon., 18; 10.00	Poliomyelitis	Dr. F. M. R. Walshe
2.15 ..	Endocrinology (Clinical) ..	Dr. R. D. Lawrence
Tues., 19; 10.00	The Decline of Infant Mortality	Sir Allen Daley
5.00 ..	Burns	Dr. L. Colebrook
Wed., 20; 10.00	Peptic Ulcer	Sir Henry Cohen
2.15 ..	Endocrinology (Experimental)	Dr. A. S. Parkes
Thurs., 21; 10.00	Nutrition and the B Vitamins	Lord Horder
2.00 ..	Neurosurgery	Sir Hugh Cairns
Fri., 22; 10.00	Cardiovascular Disease in an Ageing Population	Dr. J. H. Sheldon
2.15 ..	Orthopaedics	Mr. S. L. Higgs
Mon., 25; 10.00	Cortisone and A.C.T.H. ..	Professor G. R. Cameron
4.00 ..	Vascular System (Physiology)	Lord Horder
Tues., 26; 10.00	Early Diagnosis of Mental Disorders	Dr. Desmond Curran
4.30 ..	Tropical Medicine	Sir Philip Manson-Bahr
Wed., 27; 4.30	Epidemiology	Dr. W. H. Bradley
Thurs., 28; 10.00	Carcinoma of the Lung ..	Mr. T. Holmes Sellors
2.15 ..	Thoracic Surgery	Mr. R. C. Brock
Fri., 29 ..	—	—

JULY

Mon., 9; 4.00 ..	Odontology	Sir William Kelsey Fry

Application form for tickets is enclosed loose.

PROGRAMME OF SYMPOSIA

Monday, June 4

2 p.m.—THE PERIPHERAL NERVOUS SYSTEM. *Chairman*, Sir HENRY DALE, O.M., G.B.E., M.D., F.R.S. Professor G. L. BROWN, Transmission in Sympathetic Ganglia; Dr. W. S. FELDBERG, Special Problems of Neuromuscular Transmission; Dr. B. KATZ, The Electric Response of the Motor-end Plate; Professor J. H. BURN, The Relation of *Nor*-adrenaline to Adrenaline; Professor J. Z. YOUNG, Determination of the Size of Nerve Fibres; Mr. H. J. SEDDON, Recent Advances in the Repair of Injured Nerves; Professor GRAHAM WEDDELL, The Anatomy of Pain Sensibility.

Wednesday, June 6

10.30 a.m.—OTORHINOLARYNGOLOGY. *Chairman*, W. M. MOLLISON, C.B.E., M.Ch. *Recent Advances in Otology.* (1) Hearing-aids: Dr. T. S. LITTLER, The Development of the Medresco Aid; Mr. J. OTTY, Clinical Experiences with the Medresco Aid; Mr. P. G. GRAY, The Medresco Aid in Use—Patients' Experiences. (2) Hearing Tests: Mr. C. S. HALLPIKE, The Clinical Tests of Cochlear Function, Recent Developments of Theory and Practice. (3) The Surgery of the Labyrinth, by Mr. TERENCE CAWTHORNE.

2.30 p.m.—*Malignant Disease of the Upper Respiratory Passages.* Mr. F. C. W. CAPPS, Malignant Disease of the Nose and Paranasal Sinuses; Professor F. C. ORMEROD, Malignant Disease of the Nasopharynx and Oropharynx; Mr. V. E. NEGUS, Malignant Disease of the Pharyngo-larynx and Larynx; Dr. H. A. LUCAS, The Pathology of Malignant Disease of the Upper Respiratory Passages; Dr. GWEN HILTON and Mr. T. M. PROSSOR, The Radio-therapy of Malignant Disease of the Upper Respiratory Passages.

Thursday, June 7

2.15 p.m.—ANTIBIOTICS. *Chairman*, Professor Sir ALEXANDER FLEMING, F.R.C.S., F.R.S. Professor Sir HOWARD FLOREY, Some Observations on the Antimicrobial Products of Fungi and Bacteria; Dr. E. P. ABRAHAM, Some Chemical Aspects of Antibiotics from Fungi and Bacteria; Dr. E. LESTER SMITH, The Production of Antibiotics; Professor L. P. GARROD, Acquired Resistance to Antibiotics; Professor CLIFFORD WILSON, Clinical Evaluation of Antibiotic Therapy; Dr. G. L. M. MCELLIGOTT, Antibiotics in Venereal Disease; Professor ROBERT CRUICKSHANK, Antibiotics in Infectious Disease.

Friday, June 8

4 p.m.—THE VASCULAR SYSTEM (Clinical). *Chairman* (to be announced later). Sir JAMES LEARMONTH, Surgery of the Arteries; Professor J. MCMICHAEL, Cardiac Failure; Dr. R. T. GRANT, Wound Shock; Professor G. W. PICKERING, Essential Hypertension.

Monday, June 11

2.30 p.m.—OPHTHALMOLOGY. *Chairman* (to be announced later). Dr. L. C. THOMSON, Colour Vision; Dr. W. A. H. RUSHTON, Electrophysiology of the Retina; Mr. B. W. RYCROFT, Corneal Grafts (with film); Mr. A. G. CROSS, Contact Lenses; Professor ARNOLD SORSBY, Genetics in Ophthalmology.

Tuesday, June 12

10.30 a.m.—PLASTIC SURGERY. *Chairman*, Sir GORDON GORDON-TAYLOR, K.B.E., M.S. Sir HAROLD GILLIES, General Review; Sir WILLIAM KELSEY FRY, The External Ear; Mr. RAINSFORD MOWLEM, Report on the Development of the Cancellous Chip Bone Graft.

2 p.m.—PLASTIC SURGERY (*cont.*). *Chairman*, Professor Sir JAMES PATERSON ROSS, K.C.V.O., M.S. Professor T. POMFRET KILNER, Congenital Clefts of the Lip and Palate; Sir ARCHIBALD MCINDOE, Reconstruction of the Burned Face; Mr. RAINSFORD MOWLEM and Mr. L. W. PLEWES, Orthoplastics in Industry.

Thursday, June 14

2 p.m.—THE CENTRAL NERVOUS SYSTEM. *Chairman*, W. RUSSELL BRAIN, D.M., P.R.C.P. Professor W. E. LE GROS CLARK, The Contribution of Anatomy to Problems of Sensory Discrimination; Professor E. G. T. LIDDELL, Stimulation of the Motor Cortex in Monkeys; Dr. F. M. R. WALSHE, Some Principles Governing the Interpretation of Experimental Studies of Cortical Function, with Special Reference to the Organization of Movements; Dr. GREY WALTER, The Physiology of Adaptive Behaviour.

Friday, June 15

4.30 p.m.—ANAESTHETICS. *Chairman*, I. W. MAGILL, C.V.O., M.B., D.A. Professor E. A. PASK, Research; Dr. JOHN GILLIES and Dr. G. E. H. ENDERBY, Controlled Circulation; Dr. CECIL GRAY, Relaxants; Dr. W. W. MUSHIN, Supplementary Agents; Dr. M. D. NOSWORTHY, Thoracic Surgery; Dr. A. I. PARRY BROWN, Cardiac Surgery.

Monday, June 18

10 a.m.—POLIOMYELITIS. *Chairman*, F. M. R. WALSHE, O.B.E., M.D., F.R.S. Dr. W. H. KELLEHER, Treatment of the Acute Phase; Dr. D. MCALPINE, The Early Diagnosis; Dr. F. O. MACCALLUM, Virus Infection; Dr. A. H. GALE, Poliomyelitis as an Epidemic Disease in England and Wales; Mr. H. J. SEDDON, Poliomyelitis, the Convalescent Stage.

2.15 p.m.—ENDOCRINOLOGY (Clinical). *Chairman*, R. D. LAWRENCE, M.D. Mr. L. R. BROSTER, Some Surgical Aspects of Endocrinology; Dr. R. D. LAWRENCE, Two Types of Diabetes—With and Without Blood-insulin; Dr. P. M. F. BISHOP, The Oestrogens: Their Clinical Use; Dr. LEONARD SIMPSON, Pituitary-Adrenal Hyperfunction.

Tuesday, June 19

10 a.m.—THE DECLINE OF INFANT MORTALITY. *Chairman*, Sir ALLEN DALEY, M.D., D.P.H. Sir JAMES SPENCE, Professor T. MCKEOWN, Professor T. N. JEFFCOATE, Dr. H. K. WALLER.

5 p.m.—BURNS. *Chairman*, LEONARD COLEBROOK, M.B., F.R.S. Dr. J. P. BULL, The Problem of Fluid Replacement; Dr. E. J. L. LOWBURY, The Control of Infection; Mr. DOUGLAS JACKSON, Physical Signs which Indicate the Need for Grafting; Dr. P. DALLAS ROSS, Early Skin-grafting; Mr. RAINSFORD MOWLEM, The Use of Homografts for Extensive Burns; Mr. A. B. WALLACE, The Exposure Method of Treating Burns.

Wednesday, June 20

10 a.m.—PEPTIC ULCER. *Chairman*, Professor Sir HENRY COHEN, M.D., F.R.C.P. Mr. NORMAN TANNER, The Surgeon's Viewpoint; Dr. F. AVERY JONES, The Physician's Viewpoint; Dr. COCHRANE SHANKS, Radiological Diagnosis; Dr. HENRY WILSON, Psychological Factors.

2.15 p.m.—EXPERIMENTAL ENDOCRINOLOGY. *Chairman*, A. S. PARKES, D.Sc., F.R.S. Professor E. C. DODDS, Synthetic Oestrogens; Professor F. G. YOUNG, The Endocrine Approach to the Problem of Diabetes; Dr. G. W. HARRIS, The Hypothalamo-Hypophysial Link in the Stress Syndrome; Professor E. B. VERNEY, The Excretion of Water and its Physiological Regulation; Dr. S. J. FOLLEY, Endocrine Factors in Lactation.

Thursday, June 21

10 a.m.—NUTRITION AND THE B VITAMINS. *Chairman*, The Rt. Hon. Lord HORDER, G.C.V.O., M.D. Dr. LESTER SMITH and Dr. BODLEY SCOTT, The Treatment of the Macrocytic Anaemias. Other speakers to be announced later on: B Deficiencies in the Tropics, and The Clinical Implications of Research on Vitamin B_{12}; Dr. L. J. HARRIS, Nicotinamide and Pellagra.

2 p.m.—NEUROSURGERY. *Chairman*, Professor Sir HUGH CAIRNS, K.B.E., F.R.C.S. Professor N. M. DOTT and Mr. G. L. ALEXANDER, Intracranial Aneurysmal Malformations; Professor Sir GEOFFREY JEFFERSON, The Frontal Lobe; Professor Sir HUGH CAIRNS, Head Injuries; Mr. J. B. PENNYBACKER, Abscess of the Brain; Mr. HARVEY JACKSON, Tumours of the Orbit; Dr. L. GUTTMANN, The Care of the Paraplegic Patient.

Friday, June 22

10 a.m.—THE PROBLEMS OF CARDIOVASCULAR DISEASE IN AN AGEING POPULATION. *Chairman*, J. H. SHELDON, M.D., F.R.C.P. Professor A. M. BOYD; Dr. WILLIAM EVANS, Cardiac Pain. Other speakers to be announced later.

2.15 p.m.—ORTHOPAEDICS. *Chairman*, S. L. HIGGS, F.R.C.S., President, British Orthopaedic Association. Sir HARRY PLATT, Unusual Malignant Tumours of Bone. Sir GORDON GORDON-TAYLOR, The Surgery of Malignant Disease in the Vicinity of the Hip-joint; Sir THOMAS FAIRBANK, Some General Affections of the Skeleton; Mr. BRYAN MCFARLAND, Developmental Defects of Long Bones.

Monday, June 25

10 a.m.—CORTISONE AND A.C.T.H. *Chairman*, Professor G. R. CAMERON, F.R.C.P., F.R.S. Speaker to be announced on: The Clinical Implications of Recent Research Work on the Pituitary and Adrenal Glands; Dr. W. S. C. COPEMAN and Dr. OSWALD SAVAGE, The Rheumatic Diseases. Speaker to be announced on: Cortisone in the Treatment of Ophthalmic Conditions; Dr. D. LONG, Cortisone and Allergy. Speakers to be announced on: Acute Disseminated Lupus Erythematosus, and The Toxaemias of Pregnancy.

4 p.m.—THE PHYSIOLOGY OF THE VASCULAR SYSTEM. *Chairman*, The Rt. Hon. Lord HORDER, G.C.V.O., M.D. Professor K. J. FRANKLIN, The Change-over in the Circulation During and Shortly After Birth; Professor I. DE BURGH DALY, The Pulmonary Circulation; Dr. D. A. MCDONALD and Dr. J. M. POTTER, Some Remarks on Circulatory Rheology, with the Following Films: (*a*) Blood Streams in the Basilar Artery, (*b*) Velocity of the Blood Flow in the Basilar Artery; Professor J. TRUETA, The Renal Circulation; Professor H. BARCROFT, The Action of Adrenaline and *Nor*adrenaline on the Human Circulation.

Tuesday, June 26

10 a.m.—EARLY DIAGNOSIS OF MENTAL DISORDERS. *Chairman*, DESMOND CURRAN, F.R.C.P., D.P.M. Dr. NOEL HARRIS, The Psychiatrist's Viewpoint; Dr. ROWLAND HILL, The Neurologist's Viewpoint; Dr. THOMAS BEATON, The Mental Hospital in Relation to the General Public.

4.30 p.m.—TROPICAL MEDICINE. *Chairman*, Sir PHILIP MANSON-BAHR, C.M.G., F.R.C.P. Professor H. E. SHORTT, Protozoology and World Economic Problems; Professor B. G. MAEGRAITH, Physiological Approach to Tropical Medicine; Sir NEIL HAMILTON FAIRLEY, Chemotherapy in the Control and Treatment of Malaria.

Wednesday, June 27

4.30 p.m.—EPIDEMIOLOGY. *Chairman*, W. H. BRADLEY, D.M. Dr. C. H. ANDREWES, Influenza and the Common Cold; Dr. W. N. PICKLES, Virus Diseases in General Practice.

Thursday, June 28

10 a.m.—CARCINOMA OF THE LUNG. *Chairman*, T. HOLMES SELLORS, M.Ch. Mr. R. C. BROCK, Professor D. W. SMITHERS, Dr. J. G. SCADDING, Dr. W. R. S. DOLL.

2.15 p.m.—THORACIC SURGERY. *Chairman*, R. C. BROCK. Mr. P. R. ALLISON, The Anatomy and Physiology of the Oesophagogastric Junction in Relation to Hiatal Hernia and Oesophageal Ulceration; Mr. C. PRICE THOMAS, The Surgery of Adenoma of the Bronchus; Mr. R. C. BROCK, Intracardiac Surgery.

Monday, July 9

4 p.m.—ODONTOLOGY. *Chairman*, Sir WILLIAM KELSEY FRY, C.B.E., M.D.S., F.D.S. *The Significance of Dental Sepsis to the Physician, the Ear, Nose, and Throat Surgeon, the Ophthalmologist, and the Dermatologist.* The Physician, Dr. A. H. DOUTHWAITE; The Ear, Nose, and Throat Surgeon, Mr. C. GILL-CAREY. Speaker to be announced on: The Ophthalmologist. The Dermatologist, Dr. W. J. O'DONOVAN. The subsequent discussion will be opened by Dr. WILFRED FISH and Mr. MARTIN RUSHTON.

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